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Results of your search request

Monkey Pox

ID of request: 35783
Date of request: 19th May, 2022
Date of completion: 23rd May, 2022

If you would like to request any articles or any further help, please contact: Sarah Rudd at Sarah.Rudd@nbt.nhs.uk

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Sources searched
BMJ Best Practice (1)
DynaMed (1)
European Centre for Disease Prevention and Control (ECDC) (2)
UK H (1)
UK Health Security Agency (UKHSA) (1)
World Health Organization (1)

Date range used (5 years, 10 years): 2017-present
Limits used (gender, article/study type, etc.): -
Search terms and notes (full search strategy for database searches below):

Google Search strategies:

monkeypox domain:gov.uk (20/05/2022)

monkeypox domain:nhs.uk (20/05/2022)

monkeypox (20/05/2022)

For more information about the resources please go to:
https://link.nbt.nhs.uk/Interact/Pages/Section/Default.aspx?Section=3527 .

Summary of Results

This document pulls together the latest information on monkeypox, from the WHO, The UK Health Security Agency, and relevant evidence from journal articles. Also included are relevant subject summaries from DynaMed and BMJ Best Practice which have been recently updated.

Contents

European Centre for Disease Prevention and Control (ECDC)
Factsheet for health professionals on monkeypox

UK Health Forum
Monkeypox cases confirmed in England – latest updates

UK Health Security Agency (UKHSA)
Monkeypox

B. Synopses or Summaries

BMJ Best Practice
Poxvirus infection

DynaMed
Smallpox

European Centre for Disease Prevention and Control (ECDC)
Monkeypox cases reported in UK and Portugal News

World Health Organization (WHO)
Monkeypox

C. Systematic Reviews

Expert review of anti-infective therapy
An overview of tecovirimat for smallpox treatment and expanded anti-orthopoxvirus applications.
Monkeypox re-emergence in Africa: a call to expand the concept and practice of One Health.

Frontiers in public health
Emergence of Monkeypox as the Most Important Orthopoxvirus Infection in Humans.

Infectious disease clinics of North America
Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention.

International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases
Monkeypox - Enhancing public health preparedness for an emerging lethal human zoonotic epidemic threat in the wake of the smallpox post-eradication era.

Journal of medical virology
A review of the monkeypox virus and a recent outbreak of skin rash disease in Nigeria.

Medecine et sante tropicales
Review of poxvirus: emergence of monkeypox.

PLoS neglected tropical diseases
The changing epidemiology of human monkeypox-A potential threat? A systematic review.
A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy.

Viruses
Here, There, and Everywhere: The Wide Host Range and Geographic Distribution of Zoonotic Orthopoxviruses.

Monkeypox Virus in Nigeria: Infection Biology, Epidemiology, and Evolution.
Modulating Vaccinia Virus Immunomodulators to Improve Immunological Memory.
Improving the Care and Treatment of Monkeypox Patients in Low-Resource Settings: Applying Evidence from Contemporary Biomedical and Smallpox Biodefense Research.

Wilderness & environmental medicine
The Disease Ecology, Epidemiology, Clinical Manifestations, Management, Prevention, and Control of Increasing Human Infections with Animal Orthopoxviruses.

D. Original Research

1. Exportation of Monkeypox Virus From the African Continent.
2. Imported Monkeypox From International Traveler, Maryland, United States, 2021.
3. Imported Monkeypox from International Traveler, Maryland, USA, 2021.
4. Monkeypox in a Traveler Returning from Nigeria - Dallas, Texas, July 2021.
5. Seven monkeypox cases are confirmed in England.
6. (+)-Camphor and (-)-borneol derivatives as potential anti-orthopoxvirus agents.
7. A human recombinant analogue to plasma-derived vaccinia immunoglobulin prophylactically and therapeutically protects against lethal orthopoxvirus challenge.
8. Clinical and Epidemiological Findings from Enhanced Monkeypox Surveillance in Tshuapa Province, Democratic Republic of the Congo During 2011-2015.
9. Family cluster of three cases of monkeypox imported from Nigeria to the United Kingdom, May 2021.
10. Genomic history of human monkey pox infections in the Central African Republic between 2001 and 2018.
11. Human Monkey Pox Virus Infection in Plateau State, North Central Nigeria: A Report of Two Cases.
12. iCAT: diagnostic assessment tool of immunological history using high-throughput T-cell receptor sequencing.
13. Monkeypox.
14. New methylene blue derivatives suggest novel anti-orthopoxviral strategies.
15. Re-Emergence of monkeypox amidst delta variant concerns: A point of contention for public health virology?.
16. Reemergence of Human Monkeypox and Declining Population Immunity in the Context of Urbanization, Nigeria, 2017-2020.
17. The Evolving Epidemiology of Human Monkeypox: Questions Still to Be Answered.
18. Transmission dynamics of Monkeypox virus: a mathematical modelling approach.
19. A Case Report of Monkeypox in a 4-Year-Old Boy from the DR Congo: Challenges of Diagnosis and Management.
20. A game-theoretic model of Monkeypox to assess vaccination strategies.
21. A Tale of Two Viruses: Coinfections of Monkeypox and Varicella Zoster Virus in the Democratic Republic of Congo.
22. Acceptance and willingness to pay for a hypothetical vaccine against monkeypox viral infection among frontline physicians: A cross-sectional study in Indonesia.
23. An adult patient with suspected of monkeypox infection differential diagnosed to chickenpox.
24. Assessment of media reportage of monkeypox in southern Nigeria.
25. Asymptomatic Orthopoxvirus Circulation in Humans in the Wake of a Monkeypox Outbreak among Chimpanzees in Cameroon.
26. Clinical Course and Outcome of Human Monkeypox in Nigeria.
27. Confidence in managing human monkeypox cases in Asia: A cross-sectional survey among general practitioners in Indonesia.
28. CRISPR/Cas9 as an antiviral against Orthopoxviruses using an AAV vector.
29. Do Monkeypox Exposures Vary by Ethnicity? Comparison of Aka and Bantu Suspected Monkeypox Cases.
30. Human monkeypox - After 40 years, an unintended consequence of smallpox eradication.
31. Human-to-Human Transmission of Monkeypox Virus, United Kingdom, October 2018.

32. Identification and Whole-Genome Sequencing of a Monkeypox Virus Strain Isolated in Israel.
33. Identification of protective T-cell antigens for smallpox vaccines.
34. Importance of epidemiological research of monkeypox: is incidence increasing?.
35. Knowledge of human monkeypox viral infection among general practitioners: a cross-sectional study in Indonesia.
36. Misinformation making a disease outbreak worse: outcomes compared for influenza, monkeypox, and norovirus.
37. Modelling human-to-human transmission of monkeypox.
38. Monitoring healthcare professionals after monkeypox exposure: Experience from the first case imported to Asia.
39. Monkeypox Rash Severity and Animal Exposures in the Democratic Republic of the Congo.
40. Use of Surveillance Outbreak Response Management and Analysis System for Human Monkeypox Outbreak, Nigeria, 2017-2019.
41. A case of imported Monkeypox in Singapore.
42. Diagnosis of Imported Monkeypox, Israel, 2018.
43. Emergence of human monkeypox in west Africa.
44. Epidemiologic and Ecologic Investigations of Monkeypox, Likouala Department, Republic of the Congo, 2017.
45. Human Monkeypox in Sierra Leone after 44-Year Absence of Reported Cases.
46. Intrafamily Transmission of Monkeypox Virus, Central African Republic, 2018.
47. Lay media reporting of monkeypox in Nigeria.
48. Molecular Evidence of Human Monkeypox Virus Infection, Sierra Leone.
49. Monkeypox transmission among international travellers-serious monkey business?.
50. Monkeypox virus phylogenetic similarities between a human case detected in Cameroon in 2018 and the 2017-2018 outbreak in Nigeria.
51. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report.
52. Preliminary Screening and In Vitro Confirmation of Orthopoxvirus Antivirals.
53. Recombinase polymerase amplification assay for rapid detection of Monkeypox virus.
54. Temporal and Spatial Dynamics of Monkeypox in Democratic Republic of Congo, 2000-2015.
55. The 2017 human monkeypox outbreak in Nigeria-Report of outbreak experience and response in the Niger Delta University Teaching Hospital, Bayelsa State, Nigeria.
56. Vaccinating against monkeypox in the Democratic Republic of the Congo.
57. [Human poxvirus infections].
58. Assessing the Surveillance System for Priority Zoonotic Diseases in the Democratic Republic of the Congo, 2017.
59. Emergence of Monkeypox - West and Central Africa, 1970-2017.
60. Emergence of monkeypox in West Africa and Central Africa, 1970-2017.
61. Evolution of Synonymous Codon Usage Bias in West African and Central African Strains of Monkeypox Virus.
62. Genomic characterisation of human monkeypox virus in Nigeria.
63. Ghosts of infections past: using archival samples to understand a century of monkeypox virus prevalence among host communities across space and time.
64. Investigation of an outbreak of monkeypox in an area occupied by armed groups, Central African Republic.
65. Monkeypox contacts: a puzzling problem.
66. Notes from the Field: Responding to an Outbreak of Monkeypox Using the One Health Approach - Nigeria, 2017-2018.
67. Oral Tecovirimat for the Treatment of Smallpox.
68. Reemergence of Human Monkeypox in Nigeria, 2017.
69. Should we be already worried about Monkeypox?.
70. Sixty seconds on . . . monkeypox.
71. Sounding the alarm: Defining thresholds to trigger a public health response to monkeypox.
72. Strengthening of Surveillance during Monkeypox Outbreak, Republic of the Congo, 2017.
73. Two cases of monkeypox imported to the United Kingdom, September 2018.
74. A Nosocomial Outbreak of Human Monkeypox in the Central African Republic.
75. Enhancing case definitions for surveillance of human monkeypox in the Democratic Republic of Congo.

76. Evaluation of the GeneXpert for Human Monkeypox Diagnosis.
77. Evolution of a Disease Surveillance System: An Increase in Reporting of Human Monkeypox Disease in the Democratic Republic of the Congo, 2001-2013.
78. Frameworks for Preventing, Detecting, and Controlling Zoonotic Diseases.
79. Maternal and Fetal Outcomes Among Pregnant Women With Human Monkeypox Infection in the Democratic Republic of Congo.
80. Monkeypox Virus Host Factor Screen Using Haploid Cells Identifies Essential Role of GARP Complex in Extracellular Virus Formation.
81. Presumptive risk factors for monkeypox in rural communities in the Democratic Republic of the Congo.
82. Toward Understanding the Outcomes of Monkeypox Infection in Human Pregnancy.
83. Varicella Coinfection in Patients with Active Monkeypox in the Democratic Republic of the Congo.

A. National and International Guidance

European Centre for Disease Prevention and Control (ECDC)

Factsheet for health professionals on monkeypox (2022)

Available online at this link

Human monkeypox often begins with a combination of the following symptoms: fever, headache, chills, exhaustion, asthenia, lymph node swelling, back pain and muscle aches [15,19]. Commonly, within one to three days after onset of fever, the patient develops a rash, which tends to first appear on the face and then spreads to other parts of the body, including hands and feet [2,20-22]. The cutaneous lesions often first present as macules, evolving successively to papules, vesicles, pustules, crusts and scabs [4]. The number of lesions may range from a few to thousands [23]. Cutaneous lesions generally all appear at the same stage which is a hallmark characteristic of smallpox and MPX, and distinguishes them from chickenpox (varicella). For most people, MPX is a self-limited disease, typically lasting two to four weeks and resulting in complete recovery [21].

UK Health Forum

Monkeypox cases confirmed in England – latest updates (2022)

Available online at this link

The UK Health Security Agency (UKHSA) has detected 2 additional cases of monkeypox, one in London and one in the South East of England. The latest cases bring the total number of monkeypox cases confirmed in England since 6 May to 9, with recent cases predominantly in gay, bisexual or men who have sex with men (MSM). The 2 latest cases have no travel links to a country where monkeypox is endemic, so it is possible they acquired the infection through community transmission. The virus spreads through close contact and UKHSA is advising individuals, particularly those who are gay, bisexual or MSM, to be alert to any unusual rashes or lesions on any part of their body, especially their genitalia, and to contact a sexual health service if they have concerns. Monkeypox has not previously been described as a sexually transmitted infection, though it can be passed on by direct contact during sex. It can also be passed on through other close contact with a person who has monkeypox or contact with clothing or linens used by a

person who has monkeypox. The 2 new cases do not have known connections with previous confirmed cases announced on 16, 14 and 7 May.

UK Health Security Agency (UKHSA)

Monkeypox (2022)

Available online at this link

Monkeypox is a rare disease that is caused by infection with monkeypox virus. Monkeypox was first discovered in 1958 when outbreaks of a pox-like disease occurred in monkeys kept for research. The first human case was recorded in 1970 in the Democratic Republic of the Congo (DRC), and since then the infection has been reported in a number of central and western African countries. Most cases are reported from the DRC and Nigeria. In 2003, monkeypox was recorded in the US when an outbreak occurred following importation of rodents from Africa. Cases were reported in both humans and pet prairie dogs. All the human infections followed contact with an infected pet and all patients recovered. No other country outside West and Central Africa has reported similar outbreaks. As of 16 May, a total of 14 monkeypox cases have been reported in the UK since 2018, 7 of which have been reported in May 2022.

B. Synopses or Summaries

BMJ Best Practice

Poxvirus infection (2022)

Available online at this link

Monkeypox is a rare disease that is clinically nearly identical to smallpox, although usually less serious. There is one distinctive feature of monkeypox, which is marked lymphadenopathy.[2] The monkeypox virus can be transmitted to humans from different wild animals, such as non-human primates and rodents, although its natural host reservoir is unknown. Similar to smallpox, it can spread from human to human by the respiratory route or by direct contact with infected bodily fluids. The incubation period is usually 7 to 14 days (range 5-21 days), and disease typically lasts for 2 to 4 weeks.

DynaMed

Smallpox (2018)

Available online at this link

See sections - Differential Diagnosis; and Immunizations

European Centre for Disease Prevention and Control (ECDC)

Monkeypox cases reported in UK and Portugal News (2022)

Available online at this link

Several cases of monkeypox have been confirmed in Europe, including an EU Member State (Portugal). The first case was reported by the UK Health Security Agency (UKHSA) on 7 May and is believed to be imported. On 14 May 2022, two more cases were identified in the UK, both living in the same household, but with no recent history of travel and no contact with the case reported on 7 May. A further four cases were confirmed by UKHSA on 16 May, also without recent travel history to endemic areas, and were not contacts of the cases reported on 7 and 14 May. All cases reported on 16 May were men self-identifying as men who have sex with men (MSM). Additionally, on 18 May, Portugal reported five confirmed cases of monkeypox, and more than 20 suspected cases. All cases were young men, and all in the Lisbon and Tagus Valley. Spain has also reported eight suspected cases.

World Health Organization (WHO)

Monkeypox (2022)

Available online at this link

• Monkeypox is caused by monkeypox virus, a member of the Orthopoxvirus genus in the family Poxviridae. • Monkeypox is a viral zoonotic disease that occurs primarily in tropical rainforest areas of Central and West Africa and is occasionally exported to other regions. • Monkeypox typically presents clinically with fever, rash and swollen lymph nodes and may lead to a range of medical complications. • Monkeypox is usually a self-limited disease with the symptoms lasting from 2 to 4 weeks. Severe cases can occur. In recent times, the case fatality ratio has been around 3-6%. • Monkeypox is transmitted to humans through close contact with an infected person or animal, or with material contaminated with the virus. • Monkeypox virus is transmitted from one person to another by close contact with lesions, body fluids, respiratory droplets and contaminated materials such as bedding. • The clinical presentation of monkeypox resembles that of smallpox, a related orthopoxvirus infection which was declared eradicated worldwide in 1980. Monkeypox is less contagious than smallpox and causes less severe illness. • Vaccines used during the smallpox eradication programme also provided protection against monkeypox. Newer vaccines have been developed of which one has been approved for prevention of monkeypox • An antiviral agent developed for the treatment of smallpox has also been licensed for the treatment of monkeypox.

C. Systematic Reviews

Expert review of anti-infective therapy

An overview of tecovirimat for smallpox treatment and expanded anti-orthopoxvirus applications. (2021)

Russo Andrew T., Grosenbach Douglas W., Chinsangaram Jarasvech, Honeychurch Kady M., Long Paul G., Lovejoy Candace, Maiti Biswajit, Meara Ingrid, Hruby Dennis E.

10.1080/14787210.2020.1819791

Available online at this link

INTRODUCTION: Tecovirimat (TPOXX R; ST-246) was approved for the treatment of symptomatic smallpox by the USFDA in July of 2018 and has been stockpiled by the US government for use in a smallpox outbreak. While there has not been a reported case of smallpox since 1978 it is still considered a serious bioterrorism threat., AREAS COVERED: A brief history of smallpox from its proposed origins as a human disease through its eradication in the late 20th century is presented. The current smallpox threat and the current public health response plans are described. The discovery, and development of tecovirimat through NDA submission and subsequent approval for

treatment of smallpox are discussed. Google Scholar and PubMed were searched over all available dates for relevant publications., EXPERT OPINION: Approval of tecovirimat to treat smallpox represents an important milestone in biosecurity preparedness. Incorporating tecovirimat into the CDC smallpox response plan, development of pediatric liquid and intravenous formulations, and approval for post-exposure prophylaxis would provide additional health security benefit.Tecovirimat shows broad efficacy against orthopoxviruses in vitro and in vivo and could be developed for use against emerging orthopoxvirus diseases such as monkeypox, vaccination-associated adverse events, and side effects of vaccinia oncolytic virus therapy.

Monkeypox re-emergence in Africa: a call to expand the concept and practice of One Health. (2019)

Reynolds Mary G., Doty Jeffry B., McCollum Andrea M., Olson Victoria A., Nakazawa Yoshinori

10.1080/14787210.2019.1567330

Available online at this link

INTRODUCTION: Monkeypox is a re-emerging viral zoonosis that occurs naturally in heavily forested regions of West and Central Africa. Inter-human transmission of monkeypox virus, although limited, drives outbreaks, particularly in household and health-care settings. But the available evidence suggests that without repeated zoonotic introductions, human infections would eventually cease to occur. Therefore, interrupting virus transmission from animals to humans is key to combating this disease. Areas covered: Herein we review laboratory and field studies examining the susceptibility of various animal taxa to monkeypox virus infection, and note the competence of various species to serve as reservoirs or transmission hosts. In addition, we discuss early socio-ecologic theories of monkeypox virus transmission in rural settings and review current modes of ecologic investigation - including ecologic niche modeling, and ecologic sampling - in light of their potential to identify specific animal species and features of the environment that are associated with heightened risk for human disease. Expert opinion: The role of disease ecology and scientific research in ongoing disease prevention efforts should be reinforced, particularly for wildlife-associated zoonoses such as monkeypox. Such efforts alongside those aimed at nurturing 'One Health' collaborations may ultimately hold the greatest promise for reducing human infections with this pathogen.

Frontiers in public health

Emergence of Monkeypox as the Most Important Orthopoxvirus Infection in Humans. (2018)

Sklenovska Nikola, Van Ranst Marc

10.3389/fpubh.2018.00241

Available online at this link

Monkeypox is an emerging zoonotic disease recognized as the most important orthopoxvirus infection in humans in the smallpox post-eradication era. The clinical presentation of monkeypox is similar to the one of smallpox. The case fatality rate of monkeypox (10%) lies between the case fatality rate of variola major (30%) and variola minor (1%). The disease is endemic in the Democratic Republic of the Congo, but other countries of Central and West Africa either reported cases of monkeypox in humans or circulation in wildlife. The disease was also imported once into the USA. The disease has always been considered rare and self-limiting, however recent sporadic reports suggest otherwise. Unfortunately, the collected data is limited, dispersed and often incomplete. Therefore, the objective of this review is to trace all reported human monkeypox

outbreaks and relevant epidemiological information. The frequency and geographical spread of human monkeypox cases have increased in recent years, and there are huge gaps in our understanding of the disease's emergence, epidemiology, and ecology. The monkeypox virus is considered a high threat pathogen causing a disease of public health importance. Therefore, there is an urgent need to focus on building surveillance capacities which will provide valuable information for designing appropriate prevention, preparedness and response activities.

Infectious disease clinics of North America

Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. (2019)

Petersen Eskild, Kantele Anu, Koopmans Marion, Asogun Danny, Yinka-Ogunleye Adesola, Ihekweazu Chikwe, Zumla Alimuddin

10.1016/j.idc.2019.03.001

Available online at this link

Recently, concern has been raised about the emergence of human monkeypox virus and the occasionally severe clinical presentation bearing resemblance to that of smallpox. In 2018 3 patients in the UK were diagnosed with monkeypox, and the frequency and geographic distribution of cases across West and Central Africa have increased in recent years. In Nigeria, most monkeypox patients are aged <40 years and lack cross-protective immunity because they were born after discontinuation of the smallpox eradication campaign. This article reviews the epidemiology, clinical features, and management of monkeypox and discusses its growing public health threat in this context.

International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases

Monkeypox - Enhancing public health preparedness for an emerging lethal human zoonotic epidemic threat in the wake of the smallpox post-eradication era. (2019)

Petersen Eskild, Abubakar Ibrahim, Ihekweazu Chikwe, Heymann David, Ntoumi Francine, Blumberg Lucille, Asogun Danny, Mukonka Victor, Lule Swaib Abubaker, Bates Matthew, Honeyborne Isobella, Mfinanga Sayoki, Mwaba Peter, Dar Osman, Vairo Francesco, Mukhtar Maowia, Kock Richard, McHugh Timothy D., Ippolito Giuseppe, Zumla Alimuddin

10.1016/j.ijid.2018.11.008

Available online at this link

The identification of monkeypox in 3 separate patients in the United Kingdom in September raised media and political attention on an emerging public health threat. Nigeria, whose last confirmed case of monkeypox was in 1978, is currently experiencing an unusually large and outbreak of human monkeypox cases, a 'One Human-Environmental-Animal Health' approach is being effectively used to define and tackle the outbreak. As of 13th October 2018, there have been one hundred and sixteen confirmed cases the majority of whom are under 40 years. Over the past 20 years ten Central and West African countries have reported monkeypox cases which have risen exponentially. We review the history and evolution of monkeypox outbreaks in Africa and USA, the changing clinical presentations, and discuss possible factors underlying the increasing numbers being detected including the cessation of smallpox vaccination programs. Major knowledge gaps

remain on the epidemiology, host reservoir, and emergence, transmission, pathogenesis and prevention of monkeypoz. Copyright © 2018 The Author(s). Published by Elsevier Ltd.. All rights reserved.

Journal of medical virology

A review of the monkeypox virus and a recent outbreak of skin rash disease in Nigeria. (2019)

Kabuga Auwal I., El Zowalaty Mohamed E.

10.1002/jmv.25348

Available online at this link

Since the eradication of smallpox approximately 39 years ago, monkeypox virus remains the most pathogenic poxvirus, being mainly restricted to Central and West Africa. Before 1970, there were no reports of human monkeypox in Nigeria, while between 1971 and 1978 there were three cases, with none having been reported thereafter. However, in September 2017, a case of contagious skin rash disease, typical of monkeypox, was observed in an 11-year-old boy from the southern part of the country and confirmed to be associated with the monkeypox virus. This large outbreak consisted of 262 suspected, 115 confirmed cases, and 7 mortalities across 26 states and the Federal Capital Territory (FCT), Abuja. The aim of this manuscript is to provide an updated, comprehensive, and timely review of monkeypox, an important emerging infection in Nigeria. Monkeypox is now a major threat to global health security, requiring an urgent multidisciplinary approach involving veterinarians, physicians, virologists, and public health experts to fast-track the development of diagnostic assays, vaccines, antivirals, and other control strategies. Copyright © 2018 Wiley Periodicals, Inc.

Medecine et sante tropicales

Review of poxvirus: emergence of monkeypox. (2017)

Morand A., Delaigue S., Morand J. J

10.1684/mst.2017.0653

Available online at this link

This article reviews the different types of poxvirus infections. Smallpox, although eradicated, must continue to be monitored because of the potential risk of accidental or voluntary (by bioterrorism) reintroduction. Monkeypox and cowpox viruses are considered to be emergent today ; their high risk of dissemination is due to the increase in international transport as well as trends for new animals as pets and the loss of vaccinal protection against smallpox. Molluscum contagiosum (molluscipoxvirus) causes mild infections, is particularly frequent in children ; in adults it is a marker of the risk of sexually transmitted infections and can, in cases with profuse lesions, reveal AIDS.

PLoS neglected tropical diseases

The changing epidemiology of human monkeypox-A potential threat? A systematic review. (2022)

Bunge Eveline M., Hoet Bernard, Chen Liddy, Lienert Florian, Weidenthaler Heinz, Baer Lorraine R., Steffen Robert

10.1371/journal.pntd.0010141

Available online at this link

Monkeypox, a zoonotic disease caused by an orthopoxvirus, results in a smallpox-like disease in humans. Since monkeypox in humans was initially diagnosed in 1970 in the Democratic Republic of the Congo (DRC), it has spread to other regions of Africa (primarily West and Central), and cases outside Africa have emerged in recent years. We conducted a systematic review of peer-reviewed and grey literature on how monkeypox epidemiology has evolved, with particular emphasis on the number of confirmed, probable, and/or possible cases, age at presentation, mortality, and geographical spread. The review is registered with PROSPERO (CRD42020208269). We identified 48 peer-reviewed articles and 18 grey literature sources for data extraction. The number of human monkeypox cases has been on the rise since the 1970s, with the most dramatic increases occurring in the DRC. The median age at presentation has increased from 4 (1970s) to 21 years (2010-2019). There was an overall case fatality rate of 8.7%, with a significant difference between clades-Central African 10.6% (95% CI: 8.4%- 13.3%) vs. West African 3.6% (95% CI: 1.7%- 6.8%). Since 2003, import- and travel-related spread outside of Africa has occasionally resulted in outbreaks. Interactions/activities with infected animals or individuals are risk behaviors associated with acquiring monkeypox. Our review shows an escalation of monkeypox cases, especially in the highly endemic DRC, a spread to other countries, and a growing median age from young children to young adults. These findings may be related to the cessation of smallpox vaccination, which provided some cross-protection against monkeypox, leading to increased human-to-human transmission. The appearance of outbreaks beyond Africa highlights the global relevance of the disease. Increased surveillance and detection of monkeypox cases are essential tools for understanding the continuously changing epidemiology of this resurging disease.

A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. (2019)

Beer Ellen M., Rao V. Bhargavi

10.1371/journal.pntd.0007791

Available online at this link

Monkeypox is a vesicular-pustular illness that carries a secondary attack rate in the order of 10% in contacts unvaccinated against smallpox. Case fatality rates range from 1 to 11%, but scarring and other sequelae are common in survivors. It continues to cause outbreaks in remote populations in Central and West Africa, in areas with poor access and weakened or disrupted surveillance capacity and information networks. Recent outbreaks in Nigeria (2017-18) and Cameroon (2018) have occurred where monkeypox has not been reported for over 20 years. This has prompted concerns over whether there have been changes in the biology and epidemiology of the disease that may in turn have implications for how outbreaks and cases should best be managed. A systematic review was carried out to examine reported data on human monkeypox outbreaks over time, and to identify if and how epidemiology has changed. Published and grey literature were critically analysed, and data extracted to inform recommendations on outbreak response, use of case definitions and public health advice. The level of detail, validity of data, geographical coverage and consistency of reporting varied considerably across the 71 monkeypox outbreak documents obtained. An increase in cases reported over time was supported by literature from the Democratic Republic of Congo (DRC). Data were insufficient to measure trends in secondary attack rates and case fatality rates. Phylogenetic analyses consistently identify two strains of the virus without evidence of emergence of a new strain. Understanding of monkeypox virulence with

regard to clinical presentation by strain is minimal, with infrequent sample collection and laboratory analysis. A variety of clinical and surveillance case definitions are described in the literature: two definitions have been formally evaluated and showed high sensitivity but low specificity. These were specific to a Congo-Basin (CB) strain-affected area of the DRC where they were used. Evidence on use of antibiotics for prophylaxis against secondary cutaneous infection is anecdotal and limited. Current evidence suggests there has been an increase in total monkeypox cases reported by year in the DRC irrespective of advancements in the national Integrated Disease Surveillance and Response (IDSR) system. There has been a marked increase in number of individual monkeypox outbreak reports, from outside the DRC in between 2010 and 2018, particularly in the Central African Republic (CAR) although this does not necessarily indicate an increase in annual cases over time in these areas. The geographical pattern reported in the Nigeria outbreak suggests a possible new and widespread zoonotic reservoir requiring further investigation and research. With regards to outbreak response, increased attention is warranted for high-risk patient groups, and nosocomial transmission risks. The animal reservoir remains unknown and there is a dearth of literature informing case management and successful outbreak response strategies. Up-to-date complete, consistent and longer-term research is sorely needed to inform and guide evidence-based response and management of monkeypox outbreaks.

Viruses

Here, There, and Everywhere: The Wide Host Range and Geographic Distribution of Zoonotic Orthopoxviruses. (2020)

Silva Natalia Ingrid Oliveira, de Oliveira Jaqueline Silva, Kroon Erna Geessien, Trindade Giliane de Souza, Drumond Betania Paiva

10.3390/v13010043

Available online at this link

The global emergence of zoonotic viruses, including poxviruses, poses one of the greatest threats to human and animal health. Forty years after the eradication of smallpox, emerging zoonotic orthopoxviruses, such as monkeypox, cowpox, and vaccinia viruses continue to infect humans as well as wild and domestic animals. Currently, the geographical distribution of poxviruses in a broad range of hosts worldwide raises concerns regarding the possibility of outbreaks or viral dissemination to new geographical regions. Here, we review the global host ranges and current epidemiological understanding of zoonotic orthopoxviruses while focusing on orthopoxviruses with epidemic potential, including monkeypox, cowpox, and vaccinia viruses.

Monkeypox Virus in Nigeria: Infection Biology, Epidemiology, and Evolution. (2020)

Alakunle Emmanuel, Moens Ugo, Nchinda Godwin, Okeke Malachy Ifeanyi

10.3390/v12111257

Available online at this link

Monkeypox is a zoonotic disease caused by monkeypox virus (MPXV), which is a member of orthopoxvirus genus. The reemergence of MPXV in 2017 (at Bayelsa state) after 39 years of no reported case in Nigeria, and the export of travelers' monkeypox (MPX) from Nigeria to other parts of the world, in 2018 and 2019, respectively, have raised concern that MPXV may have emerged to occupy the ecological and immunological niche vacated by smallpox virus. This review X-rays the current state of knowledge pertaining the infection biology, epidemiology, and evolution of MPXV in Nigeria and worldwide, especially with regard to the human, cellular, and viral factors that

modulate the virus transmission dynamics, infection, and its maintenance in nature. This paper also elucidates the role of recombination, gene loss and gene gain in MPXV evolution, chronicles the role of signaling in MPXV infection, and reviews the current therapeutic options available for the treatment and prevention of MPX. Additionally, genome-wide phylogenetic analysis was undertaken, and we show that MPXV isolates from recent 2017 outbreak in Nigeria were monophyletic with the isolate exported to Israel from Nigeria but do not share the most recent common ancestor with isolates obtained from earlier outbreaks, in 1971 and 1978, respectively. Finally, the review highlighted gaps in knowledge particularly the non-identification of a definitive reservoir host animal for MPXV and proposed future research endeavors to address the unresolved questions.

Modulating Vaccinia Virus Immunomodulators to Improve Immunological Memory. (2018)

Albarnaz Jonas D., Torres Alice A., Smith Geoffrey L.

10.3390/v10030101

Available online at this link

The increasing frequency of monkeypox virus infections, new outbreaks of other zoonotic orthopoxviruses and concern about the re-emergence of smallpox have prompted research into developing antiviral drugs and better vaccines against these viruses. This article considers the genetic engineering of vaccinia virus (VACV) to enhance vaccine immunogenicity and safety. The virulence, immunogenicity and protective efficacy of VACV strains engineered to lack specific immunomodulatory or host range proteins are described. The ultimate goal is to develop safer and more immunogenic VACV vaccines that induce long-lasting immunological memory.

Improving the Care and Treatment of Monkeypox Patients in Low-Resource Settings: Applying Evidence from Contemporary Biomedical and Smallpox Biodefense Research. (2017)

Reynolds Mary G., McCollum Andrea M., Nguete Beatrice, Shongo Lushima Robert, Petersen Brett W.

10.3390/v9120380

Available online at this link

Monkeypox is a smallpox-like illness that can be accompanied by a range of significant medical complications. To date there are no standard or optimized guidelines for the clinical management of monkeypox (MPX) patients, particularly in low-resource settings. Consequently, patients can experience protracted illness and poor outcomes. Improving care necessitates developing a better understanding of the range of clinical manifestations-including complications and sequelae-as well as of features of illness that may be predictive of illness severity and poor outcomes. Experimental and natural infection of non-human primates with monkeypox virus can inform the approach to improving patient care, and may suggest options for pharmaceutical intervention. These studies have traditionally been performed to address the threat of smallpox bioterrorism and were designed with the intent of using MPX as a disease surrogate for smallpox. In many cases this necessitated employing high-dose, inhalational or intravenous challenge to recapitulate the severe manifestations of illness seen with smallpox. Overall, these data-and data from biomedical research involving burns, superficial wounds, herpes, eczema vaccinatum, and so forth-suggest that MPX patients could benefit from clinical support to mitigate the consequences of compromised skin and mucosa. This should include prevention and treatment of secondary bacterial infections (and other complications), ensuring adequate hydration and nutrition, and protecting vulnerable

anatomical locations such as the eyes and genitals. A standard of care that considers these factors should be developed and assessed in different settings, using clinical metrics specific for MPX alongside consideration of antiviral therapies.

Wilderness & environmental medicine

The Disease Ecology, Epidemiology, Clinical Manifestations, Management, Prevention, and Control of Increasing Human Infections with Animal Orthopoxviruses. (2021)

Diaz James H.

10.1016/j.wem.2021.08.003

Available online at this link

Zoonotic orthopoxvirus outbreaks have occurred repeatedly worldwide, including monkeypox in Africa and the United States, cowpox in Europe, camelpox in the Middle East and India, buffalopox in India, vaccinia in South America, and novel emerging orthopoxvirus infections in the United States, Europe, Asia, and South America. Waning smallpox immunity may increase the potential for animal-to-human transmission followed by further community transmission person-to-person (as demonstrated by monkeypox and buffalopox outbreaks) and by contact with fomites (as demonstrated by camelpox, cowpox, and, possibly, Alaskapox). The objectives of this review are to describe the disease ecology, epidemiology, clinical manifestations, prevention, and control of human infections with animal orthopoxviruses and to discuss the association with diminished population herd immunity formerly induced by vaccinia vaccination against smallpox. Internet search engines were queried with key words, and case reports, case series, seroprevalence studies, and epidemiologic investigations were found for review.

D. Original Research

1. **Exportation of Monkeypox Virus From the African Continent.**
   Mauldin Matthew R. The Journal of infectious diseases 2022;225(8):1367-1376.

   BACKGROUND: The largest West African monkeypox outbreak began September 2017, in Nigeria. Four individuals traveling from Nigeria to the United Kingdom (n = 2), Israel (n = 1), and Singapore (n = 1) became the first human monkeypox cases exported from Africa, and a related nosocomial transmission event in the United Kingdom became the first confirmed human-to-human monkeypox transmission event outside of Africa., METHODS: Epidemiological and molecular data for exported and Nigerian cases were analyzed jointly to better understand the exportations in the temporal and geographic context of the outbreak., RESULTS: Isolates from all travelers and a Bayelsa case shared a most recent common ancestor and traveled to Bayelsa, Delta, or Rivers states. Genetic variation for this cluster was lower than would be expected from a random sampling of genomes from this outbreak, but data did not support direct links between travelers., CONCLUSIONS: Monophyly of exportation cases and the Bayelsa sample, along with the intermediate levels of genetic variation, suggest a small pool of related isolates is the likely source for the exported infections. This may be the result of the level of genetic variation present in monkeypox isolates circulating within the contiguous region of Bayelsa, Delta, and Rivers states, or another more restricted, yet unidentified source pool.

   10.1093/infdis/jiaa559 this link

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2. **Imported Monkeypox From International Traveler, Maryland, United States, 2021.**
   Anonymous The Pediatric infectious disease journal 2022;41(6):489.

   10.1097/INF.0000000000003530 this link

   Available online at this link

3. **Imported Monkeypox from International Traveler, Maryland, USA, 2021.**
   Costello Varea Emerging infectious diseases 2022;28(5):1002-1005.

   A case of monkeypox was diagnosed in a returning traveler from Nigeria to Maryland, USA. Prompt infection control measures led to no secondary cases in 40 exposed healthcare workers. Given the global health implications, public health systems should be aware of effective strategies to mitigate the potential spread of monkeypox.

   10.3201/eid2805.220292 this link

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4. **Monkeypox in a Traveler Returning from Nigeria - Dallas, Texas, July 2021.**
   Rao Agam K. MMWR. Morbidity and mortality weekly report 2022;71(14):509-516.

   Monkeypox is a rare, sometimes life-threatening zoonotic infection that occurs in west and central Africa. It is caused by Monkeypox virus, an orthopoxvirus similar to Variola virus (the causative agent of smallpox) and Vaccinia virus (the live virus component of orthopoxvirus vaccines) and can spread to humans. After 39 years without detection of human disease in Nigeria, an outbreak involving 118 confirmed cases was identified during 2017-2018 (1); sporadic cases continue to occur. During September 2018-May 2021, six unrelated persons traveling from Nigeria received diagnoses of monkeypox in non-African countries: four in the United Kingdom and one each in Israel and Singapore. In July 2021, a man who traveled from Lagos, Nigeria, to Dallas, Texas, became the seventh traveler to a non-African country with diagnosed monkeypox. Among 194 monitored contacts, 144 (74%) were flight contacts. The patient received tecovirimat, an antiviral for treatment of orthopoxvirus infections, and his home required large-scale decontamination. Whole genome sequencing showed that the virus was consistent with a strain of Monkeypox virus known to circulate in Nigeria, but the specific source of the patient's infection was not identified. No epidemiologically linked cases were reported in Nigeria; no contact received postexposure prophylaxis (PEP) with the orthopoxvirus vaccine ACAM2000.

   10.15585/mmwr.mm7114a1 this link

   Available online at this link

5. **Seven monkeypox cases are confirmed in England.**
   Mahase Elisabeth BMJ (Clinical research ed.) 2022;377:o1239.

   10.1136/bmj.o1239 this link

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6. **(+)-Camphor and (-)-borneol derivatives as potential anti-orthopoxvirus agents.**
Sokolova Anastasiya S. Archiv der Pharmazie 2021;354(6):e2100038.

Although the World Health Organisation had announced that smallpox was eradicated over 40 years ago, the disease and other related pathogenic poxviruses such as monkeypox remain potential bioterrorist weapons and could also re-emerge as natural infections. We have previously reported (+)-camphor and (-)-borneol derivatives with an antiviral activity against the vaccinia virus. This virus is similar to the variola virus (VARV), the causative agent of smallpox, but can be studied at BSL-2 facilities. In the present study, we evaluated the antiviral activity of the most potent compounds against VARV, cowpox virus, and ectromelia virus (ECTV). Among the compounds tested, 4-bromo-N'-((1R,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene)benzohydrazide 18 is the most effective compound against various orthopoxviruses, including VARV, with an EC50 value of 13.9 muM and a selectivity index of 206. Also, (+)-camphor thiosemicarbazone 9 was found to be active against VARV and ECTV. Copyright © 2021 Deutsche Pharmazeutische Gesellschaft.

10.1002/ardp.202100038 this link

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7. **A human recombinant analogue to plasma-derived vaccinia immunoglobulin prophylactically and therapeutically protects against lethal orthopoxvirus challenge.**
Parker Scott Antiviral research 2021;195:105179.

Orthopoxviruses such as variola and monkeypox viruses continue to threaten the human population. Monkeypox virus is endemic in central and western Africa and outbreaks have reached as far as the U.S. Although variola virus, the etiologic agent of smallpox, has been eradicated by a successful vaccination program, official and likely clandestine stocks of the virus exist. Moreover, studies with ectromelia virus (the etiological agent of mousepox) have revealed that IL-4 recombinant viruses are significantly more virulent than wild-type viruses even in mice treated with vaccines and/or antivirals. For these reasons, it is critical that antiviral modalities are developed to treat these viruses should outbreaks, or deliberate dissemination, occur. Currently, 2 antivirals (brincidofovir and tecovirimat) are in the U.S. stockpile allowing for emergency use of the drugs to treat smallpox. Both antivirals have advantages and disadvantages in a clinical and emergency setting. Here we report on the efficacy of a recombinant immunoglobulin (rVIG) that demonstrated efficacy against several orthopoxviruses in vitro and in vivo in both a prophylactic and therapeutic fashion. A single intraperitoneal injection of rVIG significantly protected mice when given up to 14 days before or as late as 6 days post challenge. Moreover, rVIG reduced morbidity, as measured by weight-change, as well as several previously established biomarkers of disease. In rVIG treated mice, we found that vDNA levels in blood were significantly reduced, as was ALT (a marker of liver damage) and infectious virus levels in the liver. No apparent adverse events were observed in rVIG treated mice, suggesting the immunoglobulin is well tolerated. These findings suggest that recombinant immunoglobulins could be candidates for further evaluation and possible licensure under the FDA Animal Rule. Copyright © 2021. Published by Elsevier B.V.

10.1016/j.antiviral.2021.105179 this link

Available online at this link

8. **Clinical and Epidemiological Findings from Enhanced Monkeypox Surveillance in Tshuapa Province, Democratic Republic of the Congo During 2011-2015.**
Whitehouse Erin R. The Journal of infectious diseases 2021;223(11):1870-1878.

BACKGROUND: Monkeypox is a poorly described emerging zoonosis endemic to Central and Western Africa., METHODS: Using surveillance data from Tshuapa Province, Democratic Republic of the Congo during 2011-2015, we evaluated differences in incidence, exposures, and clinical presentation of polymerase chain reaction-confirmed cases by sex and age., RESULTS: We report 1057 confirmed cases. The average annual incidence was 14.1 per 100 000 (95% confidence interval, 13.3-15.0). The incidence was higher in male patients (incidence rate ratio comparing males to females, 1.21; 95% confidence interval, 1.07-1.37), except among those 20-29 years old (0.70; .51-.95). Females aged 20-29 years also reported a high frequency of exposures (26.2%) to people with monkeypox-like symptoms. The highest incidence was among 10-19-year-old males, the cohort reporting the highest proportion of animal exposures (37.5%). The incidence was lower among those presumed to have received smallpox vaccination than among those presumed unvaccinated. No differences were observed by age group in lesion count or lesion severity score., CONCLUSIONS: Monkeypox incidence was twice that reported during 1980-1985, an increase possibly linked to declining immunity provided by smallpox vaccination. The high proportion of cases attributed to human exposures suggests changing exposure patterns. Cases were distributed across age and sex, suggesting frequent exposures that follow sociocultural norms. Copyright Published by Oxford University Press for the Infectious Diseases Society of America 2021.

10.1093/infdis/jiab133 this link

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9. **Family cluster of three cases of monkeypox imported from Nigeria to the United Kingdom, May 2021.**
Hobson Gemma Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin 2021;26(32):No page numbers.

Most reported cases of human monkeypox occur in Central and West Africa, where the causing virus is endemic. We describe the identification and public health response to an imported case of West African monkeypox from Nigeria to the United Kingdom (UK) in May 2021. Secondary transmission from the index case occurred within the family to another adult and a toddler. Concurrent COVID-19-related control measures upon arrival and at the hospital, facilitated detection and limited the number of potential contacts.

10.2807/1560-7917.ES.2021.26.32.2100745 this link

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10. **Genomic history of human monkey pox infections in the Central African Republic between 2001 and 2018.**
Berthet Nicolas Scientific reports 2021;11(1):13085.

Monkeypox is an emerging infectious disease, which has a clinical presentation similar to smallpox. In the two past decades, Central Africa has seen an increase in the frequency of cases, with many monkeypox virus (MPXV) isolates detected in the Democratic Republic of Congo (DRC) and the Central African Republic (CAR). To date, no complete MPXV viral genome has been published from the human cases identified in the CAR. The objective of this study was to sequence the full genome of 10 MPXV isolates collected during the CAR

epidemics between 2001 and 2018 in order to determine their phylogenetic relationships among MPXV lineages previously described in Central Africa and West Africa. Our phylogenetic results indicate that the 10 CAR isolates belong to three lineages closely related to those found in DRC. The phylogenetic pattern shows that all of them emerged in the rainforest block of the Congo Basin. Since most human index cases in CAR occurred at the northern edge of western and eastern rainforests, transmissions from wild animals living in the rainforest is the most probable hypothesis. In addition, molecular dating estimates suggest that periods of intense political instability resulting in population movements within the country often associated also with increased poverty may have led to more frequent contact with host wild animals. The CAR socio-economic situation, armed conflicts and ecological disturbances will likely incite populations to interact more and more with wild animals and thus increase the risk of zoonotic spillover.

10.1038/s41598-021-92315-8 this link

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11. **Human Monkey Pox Virus Infection in Plateau State, North Central Nigeria: A Report of Two Cases.**
Eseigbe E. E West African journal of medicine 2021;38(12):1242-1246.

BACKGROUND: Human Monkey Pox Virus (HMPV) infection is a zoonotic infection that is endemic in the Congo basin and West Africa. Its similarity to smallpox infection, increased susceptibility infection in human populations, lack of a definitive therapy and its potential for use as a bioterrorism tool underscores its public health importance., OBJECTIVE: To describe the characteristics of HMPV infection in Plateau State, North Central Nigeria., METHODS: This was a case study of HMPV infection occurring in two Nigerian adults, seen in 2018, at Bingham University Teaching Hospital in Jos, Plateau State, Nigeria. The cases involved two siblings, and these were the first reported cases in Plateau State of Nigeria, which has an estimated population of 3.5 million persons. The diagnosis was based on a combination of clinical features and positive PCR tests on samples from the skin lesions and blood., RESULTS: The first case, a 20-year-old male, presented with a one week history of fever, headache, pain on swallowing and micturition, and generalised skin lesions. The second case is a 20 year old step brother of the first case, and the primary care provider to first case when he took ill. He also presented with a one-week history of fever, headache, pain on swallowing, and skin lesions which were less intense than in the first case. PCR assays of samples from the skin lesions and blood were positive in both cases. The other comorbidity in both cases was pharyngotonsillitis. Blood, throat, stool, and urine cultures for suspected sepsis and urinary tract infection were all negative. Both cases were admitted and discharged after receiving a course of antibiotics, antihistamine, Non-Steroidal Anti-Inflammatory Drugs, and multivitamins. Universal precautions were observed., CONCLUSION: HMPV infection in our environment underscores the need to strengthen preventive health strategies against this infection.

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12. **iCAT: diagnostic assessment tool of immunological history using high-throughput T-cell receptor sequencing.**
Rajeh Ahmad F1000Research 2021;10:65.

The pathogen exposure history of an individual is recorded in their T-cell repertoire and can be accessed through the study of T-cell receptors (TCRs) if the tools to identify them were available. For each T-cell, the TCR loci undergoes genetic rearrangement that creates a

unique DNA sequence. In theory these unique sequences can be used as biomarkers for tracking T-cell responses and cataloging immunological history. We developed the immune Cell Analysis Tool (iCAT), an R software package that analyzes TCR sequencing data from exposed (positive) and unexposed (negative) samples to identify TCR sequences statistically associated with positive samples. The presence and absence of associated sequences in samples trains a classifier to diagnose pathogen-specific exposure. We demonstrate the high accuracy of iCAT by testing on three TCR sequencing datasets. First, iCAT successfully diagnosed smallpox vaccinated versus naive samples in an independent cohort of mice with 95% accuracy. Second, iCAT displayed 100% accuracy classifying naive and monkeypox vaccinated mice. Finally, we demonstrate the use of iCAT on human samples before and after exposure to SARS-CoV-2, the virus behind the COVID-19 global pandemic. We were able to correctly classify the exposed samples with perfect accuracy. These experimental results show that iCAT capitalizes on the power of TCR sequencing to simplify infection diagnostics. iCAT provides the option of a graphical, user-friendly interface on top of usual R interface allowing it to reach a wider audience. Copyright: © 2021 Rajeh A et al.

10.12688/f1000research.27214.1 this link

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13. **Monkeypox.**
Moore Marlyn 2021;:No page numbers.

Monkeypox virus was first isolated and identified in 1958 when monkeys shipped from Singapore to a Denmark research facility fell ill.[1] However, the first confirmed human case was in 1970 when the virus was isolated from a child in the Democratic Republic of Congo suspected to have smallpox.[2] Coincident immunity to monkeypox virus was previously achieved with vaccinia vaccination; however, eradicating smallpox and subsequent lack of vaccination efforts paved the way for monkeypox to gain clinical relevance.[3] Furthermore, because most cases of monkeypox occur in rural Africa, suspected underreporting may translate to an underestimation of the potential threat of this pathogen.[4] Copyright © 2021, StatPearls Publishing LLC.

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14. **New methylene blue derivatives suggest novel anti-orthopoxviral strategies.**
Priyamvada Lalita Antiviral research 2021;191:105086.

Decades after the eradication of smallpox and the discontinuation of routine smallpox vaccination, over half of the world's population is immunologically naive to variola virus and other orthopoxviruses (OPXVs). Even in those previously vaccinated against smallpox, protective immunity wanes over time. As such, there is a concomitant increase in the incidence of human OPXV infections worldwide. To identify novel antiviral compounds with potent anti-OPXV potential, we characterized the inhibitory activity of PAV-866 and other methylene blue derivatives against the prototypic poxvirus, vaccinia virus (VACV). These compounds inactivated virions prior to infection and consequently inhibited viral binding, fusion and entry. The compounds exhibited strong virucidal activity at non-cytotoxic concentrations, and inhibited VACV infection when added before, during or after viral adsorption. The compounds were effective against other OPXVs including monkeypox virus, cowpox virus and the newly identified Akhmeta virus. Altogether, these findings reveal a novel mode of inhibition that has not previously been demonstrated for small molecule compounds against VACV. Additional studies are in progress to determine the in vivo efficacy of these compounds against OPXVs and further characterize the anti-viral

effects of these derivatives. Copyright © 2021 The Author(s). Published by Elsevier B.V. All rights reserved.

10.1016/j.antiviral.2021.105086 this link

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15. **Re-Emergence of monkeypox amidst delta variant concerns: A point of contention for public health virology?.**
Sarwar Sarosh Journal of medical virology 2021;:No page numbers.

10.1002/jmv.27306 this link

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16. **Reemergence of Human Monkeypox and Declining Population Immunity in the Context of Urbanization, Nigeria, 2017-2020.**
Nguyen Phi-Yen Emerging infectious diseases 2021;27(4):No page numbers.

A monkeypox outbreak in Nigeria during 2017-2020 provides an illustrative case study for emerging zoonoses. We built a statistical model to simulate declining immunity from monkeypox at 2 levels: At the individual level, we used a constant rate of decline in immunity of 1.29% per year as smallpox vaccination rates fell. At the population level, the cohort of vaccinated residents decreased over time because of deaths and births. By 2016, only 10.1% of the total population in Nigeria was vaccinated against smallpox; the serologic immunity level was 25.7% among vaccinated persons and 2.6% in the overall population. The substantial resurgence of monkeypox in Nigeria in 2017 appears to have been driven by a combination of population growth, accumulation of unvaccinated cohorts, and decline in smallpox vaccine immunity. The expanding unvaccinated population means that entire households, not just children, are now more susceptible to monkeypox, increasing risk of human-to-human transmission.

10.3201/eid2704.203569 this link

Available online at this link

17. **The Evolving Epidemiology of Human Monkeypox: Questions Still to Be Answered.**
Heymann David L. The Journal of infectious diseases 2021;223(11):1839-1841.

10.1093/infdis/jiab135 this link

Available online at this link

18. **Transmission dynamics of Monkeypox virus: a mathematical modelling approach.**
Peter Olumuyiwa James Modeling earth systems and environment 2021;:1-12.

Monkeypox (MPX), similar to both smallpox and cowpox, is caused by the monkeypox virus (MPXV). It occurs mostly in remote Central and West African communities, close to tropical rain forests. It is caused by the monkeypox virus in the Poxviridae family, which belongs to

the genus Orthopoxvirus. We develop and analyse a deterministic mathematical model for the monkeypox virus. Both local and global asymptotic stability conditions for disease-free and endemic equilibria are determined. It is shown that the model undergo backward bifurcation, where the locally stable disease-free equilibrium co-exists with an endemic equilibrium. Furthermore, we determine conditions under which the disease-free equilibrium of the model is globally asymptotically stable. Finally, numerical simulations to demonstrate our findings and brief discussions are provided. The findings indicate that isolation of infected individuals in the human population helps to reduce disease transmission. Copyright © The Author(s), under exclusive licence to Springer Nature Switzerland AG 2021.

10.1007/s40808-021-01313-2 this link

Available online at this link

19. **A Case Report of Monkeypox in a 4-Year-Old Boy from the DR Congo: Challenges of Diagnosis and Management.**
Eltvedt Anna Korsgaard Case reports in pediatrics 2020;2020:8572596.

Monkeypox (MP) is a rare zoonotic disease that most commonly transmits from bush animals to humans in the Congo Basin of Africa. However, an increase in cases of MP has been observed over the past decades with frequent outbreaks as well as export of the disease out of the African continent. MP belongs to the same genus of viruses as smallpox, the Orthopoxvirus, and vaccination against smallpox gives some protection against MP. With the eradication of smallpox in 1980, vaccination against smallpox has ceased. The resulting decrease of immunity against Orthopoxvirus is thought to be related to the increase in MP cases. Furthermore, closer contact between humans and bush animals could play a role along with the ongoing difficulties of controlling HIV in the same geographical area. MP remains a diagnostic challenge. Lack of knowledge about the disease among health personnel plays an important role, as well as access to diagnostic tools is limited. Treatment of MP is for now symptomatic. We report the case of a 4-year-old boy from the DR Congo with the clinical diagnosis of MP. This case illustrates some of the abovementioned challenges related to the management of MP in the field. Copyright © 2020 Anna Korsgaard Eltvedt et al.

10.1155/2020/8572596 this link

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20. **A game-theoretic model of Monkeypox to assess vaccination strategies.**
Bankuru Sri Vibhaav PeerJ 2020;8:e9272.

Monkeypox (MPX) is a zoonotic disease similar to smallpox. Its fatality rate is about 11% and it is endemic to the Central and West African countries. In this paper, we analyze a compartmental model of MPX dynamics. Our goal is to see whether MPX can be controlled and eradicated by voluntary vaccinations. We show that there are three equilibria-disease free, fully endemic and previously neglected semi-endemic (with disease existing only among humans). The existence of semi-endemic equilibrium has severe implications should the MPX virus mutate to increased viral fitness in humans. We find that MPX is controllable and can be eradicated in a semi-endemic equilibrium by vaccination. However, in a fully endemic equilibrium, MPX cannot be eradicated by vaccination alone. Copyright ©2020 Bankuru et al.

10.7717/peerj.9272 this link

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21. **A Tale of Two Viruses: Coinfections of Monkeypox and Varicella Zoster Virus in the Democratic Republic of Congo.**
Hughes Christine M. The American journal of tropical medicine and hygiene 2020;104(2):604-611.

Recent enhanced monkeypox (MPX) surveillance in the Democratic Republic of Congo, where MPX is endemic, has uncovered multiple cases of MPX and varicella zoster virus (VZV) coinfections. The purpose of this study was to verify if coinfections occur and to characterize the clinical nature of these cases. Clinical, epidemiological, and laboratory results were used to investigate MPX/VZV coinfections. A coinfection was defined as a patient with at least one Orthopoxvirus/MPX-positive sample and at least one VZV-positive sample within the same disease event. Between September 2009 and April 2014, 134 of the 1,107 (12.1%) suspected MPX cases were confirmed as MPX/VZV coinfections. Coinfections were more likely to report symptoms than VZV-alone cases and less likely than MPX-alone cases. Significantly higher lesion counts were observed for coinfection cases than for VZV-alone but less than MPX-alone cases. Discernible differences in symptom and rash severity were detected for coinfection cases compared with those with MPX or VZV alone. Findings indicate infection with both MPX and VZV could modulate infection severity. Collection of multiple lesion samples allows for the opportunity to detect coinfections. As this program continues, it will be important to continue these procedures to assess variations in the proportion of coinfected cases over time.

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22. **Acceptance and willingness to pay for a hypothetical vaccine against monkeypox viral infection among frontline physicians: A cross-sectional study in Indonesia.**
Harapan Harapan Vaccine 2020;38(43):6800-6806.

BACKGROUND: A clinical trial is ongoing to evaluate the safety and efficacy of a monkeypox vaccine among healthcare workers (HCWs). The critical question that needs to be addressed is whether HCWs are willing to accept and purchase this vaccine. The objective of this study was to evaluate the acceptance and willingness to pay (WTP) for the vaccine among HCWs., METHODS: From May to July 2019, a cross-sectional study was conducted among registered general practitioners (GPs) in Indonesia. A contingent valuation method was employed to evaluate the WTP. Besides acceptance and WTP, various explanatory variables were also collected and assessed. A logistic regression and a multivariable linear regression were used to explore the explanatory variables influencing acceptance and WTP, respectively., RESULTS: Among 407 respondents, 391 (96.0%) expressed acceptance of a free vaccination. The mean and median WTP was US$ 37.0(95%CI:US$ 32.76-US$ 41.23) and US$ 17.90(95%CI:US$ 17.90-US$ 17.90), respectively. In an unadjusted analysis, those 30 years old or younger had 2.94 times greater odds of vaccine acceptance compared to those who were older (95%CI: 1.07-8.08). Location of alma mater, type of workplace, length of individual medical experience, and monthly income of GPs were all significantly associated with WTP., CONCLUSION: Although the vast majority of GPs would accept a freely provided vaccine, they were also somewhat price sensitive. This finding indicates that partial subsidy maybe required to achieve high vaccine coverage, particularly among GPs at community health centres or those with a shorter duration of medical practice.

10.1016/j.vaccine.2020.08.034 this link

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23. **An adult patient with suspected of monkeypox infection differential diagnosed to chickenpox.**
Tumewu Junis Infectious disease reports 2020;12(Suppl 1):8724.

Background: Monkeypox is a zoonosis. The disease has a similar appearance to chickenpox caused by the varicella-zoster virus (VZV). On May 9th 2019, there was one laboratory-confirmed case of monkeypox reported in Singapore. A man was also suspected of having monkeypox on June 1st 2019 in Surabaya, Indonesia, a neighboring country., Objective: To report on a suspected case of monkeypox with differential diagnosis to chickenpox., Case: A 51-year-old male was suspected of having monkeypox after a differential diagnosis of chickenpox. His chief complaint was multiple blisters on his body. From the dermatological status on his facial, trunk and extremity regions, there were multiple pleiomorphic vesicles, some with umbilication, with a centripetal distribution, and crusts., Methods and Results: A PCR using VZV specific primers, followed by genome sequencing showed homologies of more than 99 % to other VZVs and less than 50% to Monkeypox sequences., Conclusion: Molecular laboratory techniques have confirmed the case as chickenpox. ©Copyright: the Author(s).

10.4081/idr.2020.8724 this link

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24. **Assessment of media reportage of monkeypox in southern Nigeria.**
Wogu Joseph Oluchukwu Medicine 2020;99(5):e17985.

Monkeypox is a zoonotic viral disease. Media campaigns are planned to create awareness about the disease. This is because mass media is often the leading source of information and mobilization during important health issues or crisis. The main objective of this study was to assess the media coverage of monkeypox outbreak in Nigeria. The study adopted a cross-sectional survey of residents in Southern Nigeria. A total of 600 respondents were sampled for this study through a multi-stage cluster random sampling technique. Research assistants helped in collecting data from respondents through structured questionnaire. The data collected was analyzed using percentages, mean score, and univariate analysis of variance (ANOVA). Respondents had little or no knowledge of monkeypox virus, its nature, mode of transmission, and prevention mechanism (2.30 +/- .918, P = .000). Respondents stated that they learnt about the virus through friends and social institutions instead of media (4.44 +/- .945, P = .006). Media failed to create effective and comprehensive awareness campaigns to mobilize the public (1.86 +/- 1.196, P = .001), while inappropriate and insufficient media programs and lack of funds were blamed for media ineffectiveness (4.18 +/- 1.352, P = .004). The outbreak of monkeypox virus is a public health concern in Nigeria. Media campaigns are planned to raise awareness about the disease; however, these campaigns have not demonstrated effectiveness in changing people's health behavior toward monkeypox. Media, health professionals, and government should synergize to promote a consistent health policy for the control and prevention of monkeypox virus.

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25. **Asymptomatic Orthopoxvirus Circulation in Humans in the Wake of a Monkeypox Outbreak among Chimpanzees in Cameroon.**
Guagliardo Sarah Anne J. The American journal of tropical medicine and hygiene 2020;102(1):206-212.

Monkeypox virus is a zoonotic Orthopoxvirus (OPXV) that causes smallpox-like illness in humans. In Cameroon, human monkeypox cases were confirmed in 2018, and outbreaks in captive chimpanzees occurred in 2014 and 2016. We investigated the OPXV serological status among staff at a primate sanctuary (where the 2016 chimpanzee outbreak occurred) and residents from nearby villages, and describe contact with possible monkeypox reservoirs. We focused specifically on Gambian rats (Cricetomys spp.) because they are recognized possible reservoirs and because contact with Gambian rats was common enough to render sufficient statistical power. We collected one 5-mL whole blood specimen from each participant to perform a generic anti-OPXV ELISA test for IgG and IgM antibodies and administered a questionnaire about prior symptoms of monkeypox-like illness and contact with possible reservoirs. Our results showed evidence of OPXV exposures (IgG positive, 6.3%; IgM positive, 1.6%) among some of those too young to have received smallpox vaccination (born after 1980, n = 63). No participants reported prior symptoms consistent with monkeypox. After adjusting for education level, participants who frequently visited the forest were more likely to have recently eaten Gambian rats (OR: 3.36, 95% CI: 1.91-5.92, P < 0.001) and primate sanctuary staff were less likely to have touched or sold Gambian rats (OR: 0.23, 95% CI: 0.19-0.28, P < 0.001). The asymptomatic or undetected circulation of OPXVs in humans in Cameroon is likely, and contact with monkeypox reservoirs is common, raising the need for continued surveillance for human and animal disease.

10.4269/ajtmh.19-0467 this link

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26. **Clinical Course and Outcome of Human Monkeypox in Nigeria.**
Ogoina Dimie Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2020;71(8):e210-e214.

In a retrospective review of hospital records of 40 human monkeypox cases from Nigeria, the majority developed fever and self-limiting vesiculopustular skin eruptions. Five deaths were reported. Compared to human immunodeficiency virus (HIV)-negative cases, HIV type 1-coinfected cases had more prolonged illness, larger lesions, and higher rates of both secondary bacterial skin infections and genital ulcers.

10.1093/cid/ciaa143 this link

Available online at this link

27. **Confidence in managing human monkeypox cases in Asia: A cross-sectional survey among general practitioners in Indonesia.**
Harapan Harapan Acta tropica 2020;206:105450.

The current re-emergence of human monkeypox (HMPX) is a global concern for endemic and non-endemic countries, but healthcare workers in some regions, like Asia, have less

experience with identifying and treating HMPX cases. This study aimed to assess the confidence and its predictors in HMPX case management among general practitioners (GPs), the frontline doctors in Indonesia, and to explore their perspectives on HMPX. Between May and July 2019, GPs in Indonesia completed an online-based survey. The questionnaire collected information on GPs' confidence, perspective, sociodemographic, workplace and professional characteristics, exposure to HMPX information and knowledge on HMPX. A logistic regression analysis was employed to explore the explanatory variables influencing the confidence and the perspective. We included 395 GPs in our analysis (77.4% out of 510 responses received) of which 10.1% and 34.9% were classified having good confidence using an 80% and 70% cut-off for confidence score, respectively. In the adjusted analysis, receiving information about HMPX during medical training was the only variable significantly associated with good confidence (adjusted odds ratio 2.74, 95% confidence interval 1.57 to 4.78 and $p < 0.001$). Approximately 73.6% and 77.9% of GPs agreed that HMPX is an important infectious disease and it has potential to detrimentally impact the Indonesian economy, respectively. In addition, 88.8% of GPs suggested that the disease should be incorporated into the National Medical Curriculum of Indonesia. In conclusion, in case of HMPX outbreak, majority of the GPs in Indonesia seem to be less confident in diagnosing and treating cases, using their current knowledge, skills and their workplace facilities. Therefore, a systematic strategy to improve their confidence in managing HMPX is required.

10.1016/j.actatropica.2020.105450 this link

Available online at this link

28. **CRISPR/Cas9 as an antiviral against Orthopoxviruses using an AAV vector.**
Siegrist Cathryn M. Scientific reports 2020;10(1):19307.

A vaccine for smallpox is no longer administered to the general public, and there is no proven, safe treatment specific to poxvirus infections, leaving people susceptible to infections by smallpox and other zoonotic Orthopoxviruses such as monkeypox. Using vaccinia virus (VACV) as a model organism for other Orthopoxviruses, CRISPR-Cas9 technology was used to target three essential genes that are conserved across the genus, including A17L, E3L, and I2L. Three individual single guide RNAs (sgRNAs) were designed per gene to facilitate redundancy in rendering the genes inactive, thereby reducing the reproduction of the virus. The efficacy of the CRISPR targets was tested by transfecting human embryonic kidney (HEK293) cells with plasmids encoding both SaCas9 and an individual sgRNA. This resulted in a reduction of VACV titer by up to 93.19% per target. Following the verification of CRISPR targets, safe and targeted delivery of the VACV CRISPR antivirals was tested using adeno-associated virus (AAV) as a packaging vector for both SaCas9 and sgRNA. Similarly, AAV delivery of the CRISPR antivirals resulted in a reduction of viral titer by up to 92.97% for an individual target. Overall, we have identified highly specific CRISPR targets that significantly reduce VACV titer as well as an appropriate vector for delivering these CRISPR antiviral components to host cells in vitro.

10.1038/s41598-020-76449-9 this link

Available online at this link

29. **Do Monkeypox Exposures Vary by Ethnicity? Comparison of Aka and Bantu Suspected Monkeypox Cases.**
Guagliardo Sarah Anne J. The American journal of tropical medicine and hygiene 2020;102(1):202-205.

In 2017, a monkeypox outbreak occurred in Likouala Department, Republic of the Congo. Many of the affected individuals were of Aka ethnicity, hunter-gatherers indigenous to Central Africa who have worse health outcomes in comparison with other forest-dwelling peoples. To test the hypothesis that Aka people have different risk factors for monkeypox, we analyzed questionnaire data for 39 suspected cases, comparing Aka and Bantu groups. Aka people were more likely to touch animal urine/feces, find dead animals in/around the home, eat an animal that was found dead, or to have been scratched or bitten by an animal ($P < 0.05$, all variables). They were also more likely to visit the forest >= once/week, sleep outside, or sleep on the ground ($P < 0.001$, all variables), providing opportunities for contact with monkeypox reservoirs during the night. The Aka and possibly other vulnerable groups may warrant special attention during educational and health promotion programs.

10.4269/ajtmh.19-0457 this link

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30. **Human monkeypox - After 40 years, an unintended consequence of smallpox eradication.**
Simpson Karl Vaccine 2020;38(33):5077-5081.

Smallpox eradication, coordinated by the WHO and certified 40 years ago, led to the cessation of routine smallpox vaccination in most countries. It is estimated that over 70% of the world's population is no longer protected against smallpox, and through cross-immunity, to closely related orthopox viruses such as monkeypox. Monkeypox is now a re-emerging disease. Monkeypox is endemic in as yet unconfirmed animal reservoirs in sub-Saharan Africa, while its human epidemiology appears to be changing. Monkeypox in small animals imported from Ghana as exotic pets was at the origin of an outbreak of human monkeypox in the USA in 2003. Travellers infected in Nigeria were at the origin of monkeypox cases in the UK in 2018 and 2019, Israel in 2018 and Singapore in2019. Together with sporadic reports of human infections with other orthopox viruses, these facts invite speculation that emergent or re-emergent human monkeypox might fill the epidemiological niche vacated by smallpox. An ad-hoc and unofficial group of interested experts met to consider these issues at Chatham House, London in June 2019, in order to review available data and identify monkeypox-related research gaps. Gaps identified by the experts included:The experts further agreed on the need for a better understanding of the genomic evolution and changing epidemiology of orthopox viruses, the usefulness of in-field genomic diagnostics, and the best disease control strategies, including the possibility of vaccination with new generation non-replicating smallpox vaccines and treatment with recently developed antivirals. Copyright © 2020.

10.1016/j.vaccine.2020.04.062 this link

Available online at this link

31. **Human-to-Human Transmission of Monkeypox Virus, United Kingdom, October 2018.**
Vaughan Aisling Emerging infectious diseases 2020;26(4):782-785.

In September 2018, monkeypox virus was transmitted from a patient to a healthcare worker in the United Kingdom. Transmission was probably through contact with contaminated bedding. Infection control precautions for contacts (vaccination, daily monitoring, staying home from work) were implemented. Of 134 potential contacts, 4 became ill; all patients survived.

10.3201/eid2604.191164 this link

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32. **Identification and Whole-Genome Sequencing of a Monkeypox Virus Strain Isolated in Israel.**
Cohen-Gihon Inbar Microbiology resource announcements 2020;9(10):No page numbers.

We report the whole-genome sequence of a monkeypox virus strain isolated in Israel. The strain was isolated in 2018 from a patient travelling back from West Africa. The virus was fully sequenced on the Illumina MiSeq and Oxford Nanopore Technologies MinION platforms. Copyright © 2020 Cohen-Gihon et al.

10.1128/MRA.01524-19 this link

Available online at this link

33. **Identification of protective T-cell antigens for smallpox vaccines.**
Ando Jun Cytotherapy 2020;22(11):642-652.

Background aims: E3L is an immediate-early protein of vaccinia virus (VV) that is detected within 0.5 h of infection, potentially before the many immune evasion genes of vaccinia can exert their protective effects. E3L is highly conserved among orthopoxviruses and hence could provide important protective T-cell epitopes that should be retained in any subunit or attenuated vaccine. We have therefore evaluated the immunogenicity of E3L in healthy VV-vaccinated donors., Methods: Peripheral blood mononuclear cells from healthy volunteers (n = 13) who had previously received a smallpox vaccine (Dryvax) were activated and expanded using overlapping E3L peptides and their function, specificity and antiviral activity was analyzed. E3L-specific T cells were expanded from 7 of 12 (58.3%) vaccinated healthy donors. Twenty-five percent of these produced CD8+ T-cell responses and 87.5% produced CD4+ T cells. We identified epitopes restricted by HLA-B35 and HLA-DR15., Results: E3L-specific T cells killed peptide-loaded target cells as well as vaccinia-infected cells, but only CD8+ T cells could prevent the spread of infectious virus in virus inhibition assays. The epitopes recognized by E3L-specific T cells were shared with monkeypox, and although there was a single amino acid change in the variola epitope homolog, it was recognized by vaccinia-specific T-cells., Conclusions: It might be important to include E3L in any deletion mutant or subunit vaccine and E3L could provide a useful antigen to monitor protective immunity in humans. Copyright 38; Gene Therapy. Published by Elsevier Inc. All rights reserved.

10.1016/j.jcyt.2020.04.098 this link

Available online at this link

34. **Importance of epidemiological research of monkeypox: is incidence increasing?.**
Ihekweazu Chikwe Expert review of anti-infective therapy 2020;18(5):389-392.

10.1080/14787210.2020.1735361 this link

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35. **Knowledge of human monkeypox viral infection among general practitioners: a cross-sectional study in Indonesia.**
Harapan Harapan Pathogens and global health 2020;114(2):68-75.

After the first, imported, laboratory-confirmed case of monkeypox in human was reported in Singapore on May 2019, countries in Asia started to strengthen disease surveillance systems. One challenge in preventing monkeypox is a lack of knowledge, particularly among healthcare workers. The aim of this study was to assess the knowledge of monkeypox among general practitioners (GPs) in Indonesia. A cross-sectional online survey was conducted. The survey collected participants' knowledge on a 21-item scale and explanatory variables. A two-step logistic regression analysis was employed to assess the predictors of knowledge of monkeypox. A total of 432 GPs were included; 10.0% and 36.5% of them had a good knowledge using an 80% and 70% cutoff point for knowledge domain, respectively. No explanatory variables were associated with knowledge when using 80% cutoff point. Using the lower cutoff, there was lower knowledge among GPs who graduated from universities located in Sumatra or other islands versus Java (adjusted odds ratio (aOR): 0.53; 95%CI: 0.28-0.97, p = 0.041) and among those were older than 30 years compared to younger GPs (aOR: 0.61; 95%CI: 0.39-0.96, p = 0.033). GPs working in private clinics had less knowledge compared to GPs in community health centers (aOR: 0.55; 95%CI: 0.31-0.99, p = 0.047). In conclusion, knowledge of monkeypox among GPs in Indonesia is relatively low in all groups. Increasing knowledge of monkeypox will be key to improving the capacity of GPs to respond to human monkeypox cases and to report into a disease surveillance system.

10.1080/20477724.2020.1743037 this link

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36. **Misinformation making a disease outbreak worse: outcomes compared for influenza, monkeypox, and norovirus.**
Brainard Julii Simulation 2020;96(4):365-374.

Health misinformation can exacerbate infectious disease outbreaks. Especially pernicious advice could be classified as "fake news": manufactured with no respect for accuracy and often integrated with emotive or conspiracy-framed narratives. We built an agent-based model that simulated separate but linked circulating contagious disease and sharing of health advice (classified as useful or harmful). Such advice has potential to influence human risk-taking behavior and therefore the risk of acquiring infection, especially as people are more likely in observed social networks to share bad advice. We test strategies proposed in the recent literature for countering misinformation. Reducing harmful advice from 50% to 40% of circulating information, or making at least 20% of the population unable to share or believe harmful advice, mitigated the influence of bad advice in the disease outbreak outcomes. How feasible it is to try to make people "immune" to misinformation or control spread of harmful advice should be explored. Copyright © The Author(s) 2019.

10.1177/0037549719885021 this link

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37. **Modelling human-to-human transmission of monkeypox.**
Grant Rebecca Bulletin of the World Health Organization 2020;98(9):638-640.

10.2471/BLT.19.242347 this link

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38. **Monitoring healthcare professionals after monkeypox exposure: Experience from the first case imported to Asia.**
Kyaw Win Mar Infection control and hospital epidemiology 2020;41(3):373-375.

10.1017/ice.2019.362 this link

Available online at this link

39. **Monkeypox Rash Severity and Animal Exposures in the Democratic Republic of the Congo.**
Doshi Reena H. EcoHealth 2020;17(1):64-73.

Experimental studies have suggested a larger inoculum of monkeypox virus may be associated with increased rash severity; however, little data are available on the relationship between specific animal exposures and rash severity in endemic regions. Using cross-sectional data from an active surveillance program conducted between 2005 and 2007 in the Sankuru Province of the Democratic Republic of the Congo, we explored the possible relationship between rash severity and exposures to rodents and non-human primates among confirmed MPX cases. Among the 223 PCR-confirmed MPX cases identified during active surveillance, the majority of cases (n = 149) presented with mild rash (5-100 lesions) and 33% had a more serious presentation (> 100 lesions). No association between exposure to rodents and rash severity was found in the multivariable analysis. Those that self-reported hunting NHP 3 weeks prior to onset of MPX symptoms had 2.78 times the odds of severe rash than those that did not report such exposure (95% CI: 1.18, 6.58). This study provides a preliminary step in understanding the association between animal exposure and rash severity and demonstrates correlation with exposure to NHPs and human MPX presentation. Additional research exploring the relationship between rash severity and NHPs is warranted.

10.1007/s10393-019-01459-7 this link

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40. **Use of Surveillance Outbreak Response Management and Analysis System for Human Monkeypox Outbreak, Nigeria, 2017-2019.**
Silenou Bernard C. Emerging infectious diseases 2020;26(2):345-349.

In November 2017, the mobile digital Surveillance Outbreak Response Management and Analysis System was deployed in 30 districts in Nigeria in response to an outbreak of monkeypox. Adaptation and activation of the system took 14 days, and its use improved timeliness, completeness, and overall capacity of the response.

10.3201/eid2602.191139 this link

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41. **A case of imported Monkeypox in Singapore.**
Ng Oon Tek The Lancet. Infectious diseases 2019;19(11):1166.

10.1016/S1473-3099(19)30537-7 this link

Available online at this link

42. **Diagnosis of Imported Monkeypox, Israel, 2018.**
Erez Noam Emerging infectious diseases 2019;25(5):980-983.

We report a case of monkeypox in a man who returned from Nigeria to Israel in 2018. Virus was detected in pustule swabs by transmission electron microscopy and PCR and confirmed by immunofluorescence assay, tissue culture, and ELISA. The West Africa monkeypox outbreak calls for increased awareness by public health authorities worldwide.

10.3201/eid2505.190076 this link

Available online at this link

43. **Emergence of human monkeypox in west Africa.**
Rezza Giovanni The Lancet. Infectious diseases 2019;19(8):797-799.

10.1016/S1473-3099(19)30281-6 this link

Available online at this link

44. **Epidemiologic and Ecologic Investigations of Monkeypox, Likouala Department, Republic of the Congo, 2017.**
Doshi Reena H. Emerging infectious diseases 2019;25(2):281-289.

Monkeypox, caused by a zoonotic orthopoxvirus, is endemic in Central and West Africa. Monkeypox has been sporadically reported in the Republic of the Congo. During March 22-April 5, 2017, we investigated 43 suspected human monkeypox cases. We interviewed suspected case-patients and collected dried blood strips and vesicular and crust specimens (active lesions), which we tested for orthopoxvirus antibodies by ELISA and monkeypox virus and varicella zoster virus DNA by PCR. An ecologic investigation was conducted around Manfouete, and specimens from 105 small mammals were tested for anti-orthopoxvirus antibodies or DNA. Among the suspected human cases, 22 met the confirmed, probable, and possible case definitions. Only 18 patients had available dried blood strips; 100% were IgG positive, and 88.9% (16/18) were IgM positive. Among animals, only specimens from Cricetomys giant pouched rats showed presence of orthopoxvirus antibodies, adding evidence to this species' involvement in the transmission and maintenance of monkeypox virus in nature.

10.3201/eid2502.181222 this link

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45. **Human Monkeypox in Sierra Leone after 44-Year Absence of Reported Cases.**
Reynolds Mary G. Emerging infectious diseases 2019;25(5):1023-1025.

We note the reemergence of human monkeypox in Sierra Leone following a 44-year absence of reported disease. The persons affected were an 11-month-old boy and, several years later, a 35-year-old man. The reappearance of monkeypox in this country suggests a need for renewed vigilance and awareness of the disease and its manifestations.

10.3201/eid2505.180832 this link

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46. **Intrafamily Transmission of Monkeypox Virus, Central African Republic, 2018.**
Besombes Camille Emerging infectious diseases 2019;25(8):1602-1604.

Monkeypox is a rare viral zoonotic disease; primary infections are reported from remote forest areas of Central and West Africa. We report an investigation of a monkeypox outbreak in Lobaye, southwest Central African Republic, in October 2018.

10.3201/eid2508.190112 this link

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47. **Lay media reporting of monkeypox in Nigeria.**
Oyebanji Oyeronke BMJ global health 2019;4(6):e002019.

10.1136/bmjgh-2019-002019 this link

Available online at this link

48. **Molecular Evidence of Human Monkeypox Virus Infection, Sierra Leone.**
Ye Fei Emerging infectious diseases 2019;25(6):1220-1222.

Monkeypox virus is a zoonotic disease endemic to Africa. In 2017, we confirmed a case of human monkeypox virus in Sierra Leone by molecular and serologic methods. Sequencing analysis indicated the virus belongs to the West African clade and data suggest it was likely transmitted by wild animals.

10.3201/eid2506.180296 this link

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49. **Monkeypox transmission among international travellers-serious monkey business?.**
Angelo Kristina M. Journal of travel medicine 2019;26(5):No page numbers.

10.1093/jtm/taz002 this link

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50. **Monkeypox virus phylogenetic similarities between a human case detected in Cameroon in 2018 and the 2017-2018 outbreak in Nigeria.**
Sadeuh-Mba Serge Alain Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases 2019;69:8-11.

A monkeypox virus was detected from a human clinical case in 2018 in Cameroon; a country where no human cases were reported since 1989. The virus exhibited close genetic relatedness with another monkeypox virus isolated in Nigeria during the 2017-2018 outbreak. Although our molecular findings argue in favor of an extension of the monkeypox outbreak from Nigeria into Cameroon, the possibility that the monkeypox virus detected could be indigenous to Cameroon cannot be ruled out. Copyright © 2019.

10.1016/j.meegid.2019.01.006 this link

Available online at this link

51. **Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report.**
Yinka-Ogunleye Adesola The Lancet. Infectious diseases 2019;19(8):872-879.

BACKGROUND: In September, 2017, human monkeypox re-emerged in Nigeria, 39 years after the last reported case. We aimed to describe the clinical and epidemiological features of the 2017-18 human monkeypox outbreak in Nigeria., METHODS: We reviewed the epidemiological and clinical characteristics of cases of human monkeypox that occurred between Sept 22, 2017, and Sept 16, 2018. Data were collected with a standardised case investigation form, with a case definition of human monkeypox that was based on previously established guidelines. Diagnosis was confirmed by viral identification with real-time PCR and by detection of positive anti-orthopoxvirus IgM antibodies. Whole-genome sequencing was done for seven cases. Haplotype analysis results, genetic distance data, and epidemiological data were used to infer a likely series of events for potential human-to-human transmission of the west African clade of monkeypox virus., FINDINGS: 122 confirmed or probable cases of human monkeypox were recorded in 17 states, including seven deaths (case fatality rate 6%). People infected with monkeypox virus were aged between 2 days and 50 years (median 29 years [IQR 14]), and 84 (69%) were male. All 122 patients had vesiculopustular rash, and fever, pruritus, headache, and lymphadenopathy were also common. The rash affected all parts of the body, with the face being most affected. The distribution of cases and contacts suggested both primary zoonotic and secondary human-to-human transmission. Two cases of health-care-associated infection were recorded. Genomic analysis suggested multiple introductions of the virus and a single introduction along with human-to-human transmission in a prison facility., INTERPRETATION: This study describes the largest documented human outbreak of the west African clade of the monkeypox virus. Our results suggest endemicity of monkeypox virus in Nigeria, with some evidence of human-to-human transmission. Further studies are necessary to explore animal reservoirs and risk factors for transmission of the virus in Nigeria., FUNDING: None. Copyright © 2019 World Health Organization. Published by Elsevier Ltd. All rights reserved. Published by Elsevier Ltd.. All rights reserved.

10.1016/S1473-3099(19)30294-4 this link

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52. **Preliminary Screening and In Vitro Confirmation of Orthopoxvirus Antivirals.**
Grosenbach Douglas W. Methods in molecular biology (Clifton, N.J.) 2019;2023:143-155.

The lack of antiviral drugs for the treatment of orthopoxvirus disease represents an unmet medical need, particularly due to the threat of variola virus (the causative agent of smallpox) as an agent of biowarfare or bioterrorism (Henderson, 283:1279-1282, 1999). In addition to variola, monkeypox, cowpox, and vaccinia viruses are orthopoxviruses of concern to human health (Lewis-Jones, 17:81-89, 2004). Smallpox vaccination, using the closely related vaccinia virus, is no longer provided to the general public leading to a worldwide population increasingly susceptible not only to variola but to monkeypox, cowpox, and vaccinia viruses as well. Orthopoxviruses share similar life cycles (Fenner et al., WHO, Geneva, 1988), and significant nucleotide and protein homology, and are immunologically cross-protective against other species within the genus, which was the basis of the highly successful vaccinia virus vaccine. These similarities also serve as the basis for screening for antivirals for dangerous pathogens such as variola and monkeypox virus using generally safer viruses such as cowpox and vaccinia. Methods for preliminary screening and initial characterization of potential orthopoxvirus antivirals in vitro, using vaccinia virus as a relatively safe surrogate for more pathogenic orthopoxviruses, are described herein. They include candidate identification in a viral cytopathic effect (CPE) assay as well as evaluation of the antiviral activity in inhibition assays to determine mean effective (or inhibitory) concentrations (EC50 or IC50). These assays were utilized in the identification and early characterization of tecovirimat (ST-246) (Yang et al., 79:13,139-13,149, 2005). These initial steps in identifying and characterizing the antiviral activity should be followed up with additional in vitro studies including specificity testing (for other orthopoxviruses and against other viruses), single-cycle growth curves, time of addition assays, cytotoxicity testing, and identification of the drug target.

10.1007/978-1-4939-9593-6_9 this link

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53. **Recombinase polymerase amplification assay for rapid detection of Monkeypox virus.**
Davi Saskia Dede Diagnostic microbiology and infectious disease 2019;95(1):41-45.

In this study, a rapid method for the detection of Central and West Africa clades of Monkeypox virus (MPXV) using recombinase polymerase amplification (RPA) assay targeting the G2R gene was developed. MPXV, an Orthopoxvirus, is a zoonotic dsDNA virus, which is listed as a biothreat agent. RPA was operated at a single constant temperature of 42degreeC and produced results within 3 to 10 minutes. The MPXV-RPA-assay was highly sensitive with a limit of detection of 16 DNA molecules/mul. The clinical performance of the MPXV-RPA-assay was tested using 47 sera and whole blood samples from humans collected during the recent MPXV outbreak in Nigeria as well as 48 plasma samples from monkeys some of which were experimentally infected with MPXV. The specificity of the MPXV-RPA-assay was 100% (50/50), while the sensitivity was 95% (43/45). This new MPXV-RPA-assay is fast and can be easily utilised at low resource settings using a solar powered mobile suitcase laboratory.

10.1016/j.diagmicrobio.2019.03.015 this link

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54. **Temporal and Spatial Dynamics of Monkeypox in Democratic Republic of Congo, 2000-2015.**
Mandja Bien-Aime Makasa EcoHealth 2019;16(3):476-487.

Monkeypox is a viral disease with a clinical presentation resembling that of smallpox. Although monkeypox is considered to be an important zoonotic viral disease, its epidemiology remains poorly understood, especially the spatial and temporal distribution of the disease. The present study examined weekly reports of monkeypox cases collected from 2000 to 2015 at the health zone scale in the Democratic Republic of Congo. SaTScan R was performed to identify spatial and temporal clusters of monkeypox cases. Significant primary spatial clusters were detected in the districts of Sankuru and Tshuapa. A centrifugal pattern was found, with significant primary spatial clusters extending over time from Sankuru and Tshuapa to several neighboring districts. Peaks of cases occurred from July to September for the 2000-2002 and 2003-2009 sub-periods and from January to March for the 2010-2015 sub-period. Despite the lack of additional data for confirmation, the increasing of monkeypox reported incidence was observed in the Democratic Republic of Congo during 2000-2015 period and this increase cannot be explain only by the improvements of surveillance systems. The detected spatial clusters were located in the dense rainforest of the Congo basin. The reasons for the excess incidence of monkeypox cases in the central region of the country are unknown, and the relative influence of ecological, environmental, and human factors on the mechanism of emergence of monkeypox has yet to be identified.

10.1007/s10393-019-01435-1 this link

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55. **The 2017 human monkeypox outbreak in Nigeria-Report of outbreak experience and response in the Niger Delta University Teaching Hospital, Bayelsa State, Nigeria.**
Ogoina Dimie PloS one 2019;14(4):e0214229.

BACKGROUND: In September 2017, Nigeria experienced a large outbreak of human monkeypox (HMPX). In this study, we report the outbreak experience and response in the Niger Delta University Teaching Hospital (NDUTH), Bayelsa state, where the index case and majority of suspected cases were reported., METHODS: In a cross-sectional study between September 25th and 31st December 2017, we reviewed the clinical and laboratory characteristics of all suspected and confirmed cases of HMPX seen at the NDUTH and appraised the plans, activities and challenges of the hospital in response to the outbreak based on documented observations of the hospital's infection control committee (IPC). Monkeypox cases were defined using the interim national guidelines as provided by the Nigerian Centre for Disease Control (NCDC)., RESULTS: Of 38 suspected cases of HMPX, 18(47.4%) were laboratory confirmed, 3(7.9%) were probable, while 17 (18.4%) did not fit the case definition for HMPX. Majority of the confirmed/probable cases were adults (80.9%) and males (80.9%). There was concomitant chicken pox, syphilis and HIV-1 infections in two confirmed cases and a case of nosocomial infection in one healthcare worker (HCW). The hospital established a make-shift isolation ward for case management, constituted a HMPX response team and provided IPC resources. At the outset, some HCWs were reluctant to participate in the outbreak and others avoided suspected patients. Some patients and their family members experienced stigma and discrimination and there were cases of refusal of isolation. Repeated trainings and collaborative efforts by all stakeholders addressed some of these challenges and eventually led to successful containment of the outbreak., CONCLUSION: While the 2017 outbreak of human monkeypox in Nigeria was contained, our report reveals gaps in outbreak response that could serve as lessons to other hospitals to strengthen epidemic preparedness and response activities in the hospital setting.

10.1371/journal.pone.0214229 this link

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56. **Vaccinating against monkeypox in the Democratic Republic of the Congo.**
Petersen Brett W. Antiviral research 2019;162:171-177.

Healthcare-associated transmission of monkeypox has been observed on multiple occasions in areas where the disease is endemic. Data collected by the US Centers for Disease Control and Prevention (CDC) from an ongoing CDC-supported program of enhanced surveillance in the Tshuapa Province of the Democratic Republic of the Congo, where the annual incidence of human monkeypox is estimated to be 3.5-5/10,000, suggests that there is approximately one healthcare worker infection for every 100 confirmed monkeypox cases. Herein, we describe a study that commenced in February 2017, the intent of which is to evaluate the effectiveness, immunogenicity, and safety of a third-generation smallpox vaccine, IMVAMUNE R, in healthcare personnel at risk of monkeypox virus (MPXV) infection. We describe procedures for documenting exposures to monkeypox virus infection in study participants, and outline lessons learned that may be of relevance for studies of other investigational medical countermeasures in hard to reach, under-resourced populations. Copyright © 2018. Published by Elsevier B.V.

10.1016/j.antiviral.2018.11.004 this link

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57. **[Human poxvirus infections].**
Bohelay G. Annales de dermatologie et de venereologie 2019;146(5):387-398.

Poxvirus (PXV) infections are a common cause of cutaneous signs. In France, certain forms of poxvirus are frequent and benign (molluscum contagiosum), while others are rare but potentially serious (cowpox virus [CPXV]). Whereas only smallpox and molluscum contagiosum viruses have a human reservoir and are transmitted between humans, most poxvirus infections are zoonoses having only animal reservoirs. Only a small number of poxviruses are responsible for infection in humans, but the increasing number of new pets, some of which are exotic, coupled with the rapid rise in international travel are creating a greater risk of transmission of zoonotic PXV to new vectors and of spread of these diseases to new regions throughout the world. In France, molluscum contagiosum, orf and milkers' nodule give rise to numerous consultations and are well known to dermatologists. However, dermatologists must also be able to identify other parapoxviruses of similar presentation to orf; thus, CPXV and monkeypox are considered potentially emergent viruses with a high risk of epidemic and spread due to increasing international transport and the loss of the maximum protection against smallpox. Finally, despite its declared eradication, smallpox is currently being monitored because of the potential risk of reintroduction, whether accidentally or deliberately through bioterrorism. Copyright © 2019 Elsevier Masson SAS. All rights reserved.

10.1016/j.annder.2019.03.001 this link

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58. **Assessing the Surveillance System for Priority Zoonotic Diseases in the Democratic Republic of the Congo, 2017.**
Stolka Kristen B. Health security 2018;16(S1):S44-S53.

High-functioning communicable disease surveillance systems are critical for public health preparedness. Countries that cannot quickly detect and contain diseases are a risk to the

global community. The ability of all countries to comply with the International Health Regulations is paramount for global health security. Zoonotic diseases can be particularly dangerous for humans. We conducted a surveillance system assessment of institutional and individual capacity in Kinshasa and Haut Katanga provinces in the Democratic Republic of the Congo for nationally identified priority zoonotic diseases (eg, viral hemorrhagic fever [VHF], yellow fever, rabies, monkeypox, and influenza monitored through acute respiratory infections). Data were collected from 79 health workers responsible for disease surveillance at 2 provincial health offices, 9 health zone offices, 9 general reference hospitals, and 18 health centers and communities. A set of questionnaires was used to assess health worker training in disease surveillance methods; knowledge of case definitions; availability of materials and tools to support timely case detection, reporting, and data interpretation; timeliness and completeness of reporting; and supervision from health authorities. We found that health workers either had not been recently or ever trained in surveillance methods and that their knowledge of case definitions was low. Timeliness and completeness of weekly notification of epidemic-prone diseases was generally well performed, but the lack of available standardized reporting forms and archive of completed forms affected the quality of data collected. Lessons learned from our assessment can be used for targeted strengthening efforts to improve global health security.

10.1089/hs.2018.0060 this link

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59. **Emergence of Monkeypox - West and Central Africa, 1970-2017.**
Durski Kara N. MMWR. Morbidity and mortality weekly report 2018;67(10):306-310.

The recent apparent increase in human monkeypox cases across a wide geographic area, the potential for further spread, and the lack of reliable surveillance have raised the level of concern for this emerging zoonosis. In November 2017, the World Health Organization (WHO), in collaboration with CDC, hosted an informal consultation on monkeypox with researchers, global health partners, ministries of health, and orthopoxvirus experts to review and discuss human monkeypox in African countries where cases have been recently detected and also identify components of surveillance and response that need improvement. Endemic human monkeypox has been reported from more countries in the past decade than during the previous 40 years. Since 2016, confirmed cases of monkeypox have occurred in Central African Republic, Democratic Republic of the Congo, Liberia, Nigeria, Republic of the Congo, and Sierra Leone and in captive chimpanzees in Cameroon. Many countries with endemic monkeypox lack recent experience and specific knowledge about the disease to detect cases, treat patients, and prevent further spread of the virus. Specific improvements in surveillance capacity, laboratory diagnostics, and infection control measures are needed to launch an efficient response. Further, gaps in knowledge about the epidemiology and ecology of the virus need to be addressed to design, recommend, and implement needed prevention and control measures.

10.15585/mmwr.mm6710a5 this link

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60. **Emergence of monkeypox in West Africa and Central Africa, 1970-2017.**
Anonymous Releve epidemiologique hebdomadaire 2018;93(11):125-32.

Available online at this link

61. **Evolution of Synonymous Codon Usage Bias in West African and Central African Strains of Monkeypox Virus.**
Karumathil Sudeesh Evolutionary bioinformatics online 2018;14:1176934318761368.

The evolution of bias in synonymous codon usage in chosen monkeypox viral genomes and the factors influencing its diversification have not been reported so far. In this study, various trends associated with synonymous codon usage in chosen monkeypox viral genomes were investigated, and the results are reported. Identification of factors that influence codon usage in chosen monkeypox viral genomes was done using various codon usage indices, such as the relative synonymous codon usage, the effective number of codons, and the codon adaptation index. The Spearman rank correlation analysis and a correspondence analysis were used for correlating various factors with codon usage. The results revealed that mutational pressure due to compositional constraints, gene expression level, and selection at the codon level for utilization of putative optimal codons are major factors influencing synonymous codon usage bias in monkeypox viral genomes. A cluster analysis of relative synonymous codon usage values revealed a grouping of more virulent strains as one major cluster (Central African strains) and a grouping of less virulent strains (West African strains) as another major cluster, indicating a relationship between virulence and synonymous codon usage bias. This study concluded that a balance between the mutational pressure acting at the base composition level and the selection pressure acting at the amino acid level frames synonymous codon usage bias in the chosen monkeypox viruses. The natural selection from the host does not seem to have influenced the synonymous codon usage bias in the analyzed monkeypox viral genomes.

10.1177/1176934318761368 this link

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62. **Genomic characterisation of human monkeypox virus in Nigeria.**
Faye Ousmane The Lancet. Infectious diseases 2018;18(3):246.

10.1016/S1473-3099(18)30043-4 this link

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63. **Ghosts of infections past: using archival samples to understand a century of monkeypox virus prevalence among host communities across space and time.**
Tiee Madeline S. Royal Society open science 2018;5(1):171089.

Infectious diseases that originate from multiple wildlife hosts can be complex and problematic to manage. A full understanding is further limited by large temporal and spatial gaps in sampling. However, these limitations can be overcome, in part, by using historical samples, such as those derived from museum collections. Here, we screened over 1000 museum specimens collected over the past 120 years to examine the historical distribution and prevalence of monkeypox virus (MPXV) in five species of African rope squirrel (Funisciurus sp.) collected across Central Africa. We found evidence of MPXV infections in host species as early as 1899, half a century earlier than the first recognized case of MPXV in 1958, supporting the suggestion that historic pox-like outbreaks in humans and non-human primates may have been caused by MPXV rather than smallpox as originally thought. MPX viral DNA was found in 93 of 1038 (9.0%) specimens from five Funisciurus species (F. anerythrus, F. carruthersi, F. congicus, F. lemniscatus and F. pyrropus), of which F. carruthersi and pyrropus had not previously been identified as potential MPXV

hosts. We additionally documented relative prevalence rates of infection in museum specimens of Funisciurus and examined the spatial and temporal distribution of MPXV in these potential host species across nearly a hundred years (1899-1993).

10.1098/rsos.171089 this link

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64. **Investigation of an outbreak of monkeypox in an area occupied by armed groups, Central African Republic.**
Kalthan E. Medecine et maladies infectieuses 2018;48(4):263-268.

BACKGROUND: Monkeypox is a zoonosis caused by an Orthopoxvirus of the Poxviridae family. Human infections are often severe and are a public health problem., PATIENTS AND METHOD: We conducted a monkeypox outbreak investigation of suspected case patients in five villages of the Alindao-Mingala Health District following blood sample confirmation of the virus by the Institut Pasteur in Bangui. We aimed to determine disease characteristics, to describe the context and the risk factors, and to measure the incidence and case fatality. Patients were reported in the villages of Rehou 4, 5, Dalakere 1, Kongbo, and Pavika from August to October 2016. Data was collected on individual records when interviewing patients or parents., RESULTS: A total of 26 patients were identified. The<10 years and 21-30 years age groups were the most affected. The overall attack rate was 5 per 1000 inhabitants and the case fatality was 7.7%. Young age and the absence of smallpox vaccination were associated with severe presentations in 87.5% of cases., CONCLUSION: The annual number of monkeypox outbreaks increases in the Central African Republic with severe presentations and a high case fatality especially in children. Reinforcing the surveillance and characterization of circulating strains will provide information on the need for vaccine production.

10.1016/j.medmal.2018.02.010 this link

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65. **Monkeypox contacts: a puzzling problem.**
The Lancet Lancet (London, England) 2018;392(10152):986.

10.1016/S0140-6736(18)32254-2 this link

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66. **Notes from the Field: Responding to an Outbreak of Monkeypox Using the One Health Approach - Nigeria, 2017-2018.**
Eteng Womi-Eteng MMWR. Morbidity and mortality weekly report 2018;67(37):1040-1041.

10.15585/mmwr.mm6737a5 this link

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67. **Oral Tecovirimat for the Treatment of Smallpox.**
Grosenbach Douglas W. The New England journal of medicine 2018;379(1):44-53.

BACKGROUND: Smallpox was declared eradicated in 1980, but variola virus (VARV), which causes smallpox, still exists. There is no known effective treatment for smallpox; therefore, tecovirimat is being developed as an oral smallpox therapy. Because clinical trials in a context of natural disease are not possible, an alternative developmental path to evaluate efficacy and safety was needed., METHODS: We investigated the efficacy of tecovirimat in nonhuman primate (monkeypox) and rabbit (rabbitpox) models in accordance with the Food and Drug Administration (FDA) Animal Efficacy Rule, which was interpreted for smallpox therapeutics by an expert advisory committee. We also conducted a placebo-controlled pharmacokinetic and safety trial involving 449 adult volunteers., RESULTS: The minimum dose of tecovirimat required in order to achieve more than 90% survival in the monkeypox model was 10 mg per kilogram of body weight for 14 days, and a dose of 40 mg per kilogram for 14 days was similarly efficacious in the rabbitpox model. Although the effective dose per kilogram was higher in rabbits, exposure was lower, with a mean steady-state maximum, minimum, and average (mean) concentration (Cmax, Cmin, and Cavg, respectively) of 374, 25, and 138 ng per milliliter, respectively, in rabbits and 1444, 169, and 598 ng per milliliter in nonhuman primates, as well as an area under the concentration-time curve over 24 hours (AUC0-24hr) of 3318 ngxhours per milliliter in rabbits and 14,352 ngxhours per milliliter in nonhuman primates. These findings suggested that the nonhuman primate was the more conservative model for the estimation of the required drug exposure in humans. A dose of 600 mg twice daily for 14 days was selected for testing in humans and provided exposures in excess of those in nonhuman primates (mean steady-state Cmax, Cmin, and Cavg of 2209, 690, and 1270 ng per milliliter and AUC0-24hr of 30,632 ngxhours per milliliter). No pattern of troubling adverse events was observed., CONCLUSIONS: On the basis of its efficacy in two animal models and pharmacokinetic and safety data in humans, tecovirimat is being advanced as a therapy for smallpox in accordance with the FDA Animal Rule. (Funded by the National Institutes of Health and the Biomedical Advanced Research and Development Authority; ClinicalTrials.gov number, NCT02474589 .).

10.1056/NEJMoa1705688 this link

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68. **Reemergence of Human Monkeypox in Nigeria, 2017.**
Yinka-Ogunleye Adesola Emerging infectious diseases 2018;24(6):1149-1151.

In Nigeria, before 2017 the most recent case of human monkeypox had been reported in 1978. By mid-November 2017, a large outbreak caused by the West African clade resulted in 146 suspected cases and 42 laboratory-confirmed cases from 14 states. Although the source is unknown, multiple sources are suspected.

10.3201/eid2406.180017 this link

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69. **Should we be already worried about Monkeypox?.**
Reina Jordi Medicina clinica 2018;151(8):320-322.

10.1016/j.medcli.2018.03.025 this link

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70. **Sixty seconds on . . . monkeypox.**
Rimmer Abi BMJ (Clinical research ed.) 2018;363:k4132.

10.1136/bmj.k4132 this link

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71. **Sounding the alarm: Defining thresholds to trigger a public health response to monkeypox.**
Guagliardo Sarah Anne J. PLoS neglected tropical diseases 2018;12(12):e0007034.

Endemic to the Democratic Republic of the Congo (DRC), monkeypox is a zoonotic disease that causes smallpox-like illness in humans. Observed fluctuations in reported cases over time raises questions about when it is appropriate to mount a public health response, and what specific actions should be taken. We evaluated three different thresholds to differentiate between baseline and heightened disease incidence, and propose a novel, tiered algorithm for public health action. Monkeypox surveillance data from Tshuapa Province, 2011-2013, were used to calculate three different statistical thresholds: Cullen, c-sum, and a World Health Organization (WHO) method based on monthly incidence. When the observed cases exceeded the threshold for a given month, that month was considered to be 'aberrant'. For each approach, the number of aberrant months detected was summed by year-each method produced vastly different results. The Cullen approach generated a number of aberrant signals over the period of consideration (9/36 months). The c-sum method was the most sensitive (30/36 months), followed by the WHO method (12/24 months). We conclude that triggering public health action based on signals detected by a single method may be inefficient and overly simplistic for monkeypox. We propose instead a response algorithm that integrates an objective threshold (WHO method) with contextual information about epidemiological and spatiotemporal links between suspected cases to determine whether a response should be operating under i) routine surveillance ii) alert status, or iii) outbreak status. This framework could be modified and adopted by national and zone level health workers in monkeypox-endemic countries. Lastly, we discuss considerations for selecting thresholds for monkeypox outbreaks across gradients of endemicity and public health resources.

10.1371/journal.pntd.0007034 this link

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72. **Strengthening of Surveillance during Monkeypox Outbreak, Republic of the Congo, 2017.**
Doshi Reena H. Emerging infectious diseases 2018;24(6):1158-1160.

Reports of 10 suspected cases of monkeypox in Likouala Department, Republic of the Congo, triggered an investigation and response in March 2017 that included community education and surveillance strengthening. Increasing numbers of outbreaks suggest that monkeypox virus is becoming a more prevalent human pathogen. Diverse approaches are necessary for disease control and prevention.

10.3201/eid2406.180248 this link

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73. **Two cases of monkeypox imported to the United Kingdom, September 2018.**
Vaughan Aisling Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin 2018;23(38):No page numbers.

In early September 2018, two cases of monkeypox were reported in the United Kingdom (UK), diagnosed on 7 September in Cornwall (South West England) and 11 September in Blackpool (North West England). The cases were epidemiologically unconnected and had recently travelled to the UK from Nigeria, where monkeypox is currently circulating. We describe the epidemiology and the public health response for the first diagnosed cases outside the African continent since 2003.

10.2807/1560-7917.ES.2018.23.38.1800509 this link

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74. **A Nosocomial Outbreak of Human Monkeypox in the Central African Republic.**
Nakoune Emmanuel Open forum infectious diseases 2017;4(4):ofx168.

An outbreak of familial monkeypox occurred in the Central African Republic in 2015/2016 by 3 transmission modes: familial, health care-related, and transport-related. Ten people (3 children and 7 adults) were infected. Most presented with cutaneous lesions and fever, and 2 children died. The viral strain responsible was a Zaire genotype strain.

10.1093/ofid/ofx168 this link

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75. **Enhancing case definitions for surveillance of human monkeypox in the Democratic Republic of Congo.**
Osadebe Lynda PLoS neglected tropical diseases 2017;11(9):e0005857.

BACKGROUND: Human monkeypox (MPX) occurs at appreciable rates in the Democratic Republic of Congo (DRC). Infection with varicella zoster virus (VZV) has a similar presentation to that of MPX, and in areas where MPX is endemic these two illnesses are commonly mistaken. This study evaluated the diagnostic utility of two surveillance case definitions for MPX and specific clinical characteristics associated with laboratory-confirmed MPX cases., METHODOLOGY/PRINCIPAL FINDINGS: Data from a cohort of suspect MPX cases (identified by surveillance over the course of a 42 month period during 2009-2014) from DRC were used; real-time PCR diagnostic test results were used to establish MPX and VZV diagnoses. A total of 333 laboratory-confirmed MPX cases, 383 laboratory-confirmed VZV cases, and 36 cases that were determined to not be either MPX or VZV were included in the analyses. Significant ($p<0.05$) differences between laboratory-confirmed MPX and VZV cases were noted for several signs/symptoms including key rash characteristics. Both surveillance case definitions had high sensitivity and low specificities for individuals that had suspected MPX virus infections. Using 12 signs/symptoms with high sensitivity and/or specificity values, a receiver operator characteristic analysis showed that models for MPX cases that had the presence of 'fever before rash' plus at least 7 or 8 of the 12 signs/symptoms demonstrated a more balanced performance between sensitivity and specificity., CONCLUSIONS: Laboratory-confirmed MPX and VZV cases presented with many of the same signs and symptoms, and the analysis here emphasized the utility of including 12 specific signs/symptoms when investigating MPX cases. In order to document and detect endemic human MPX cases, a surveillance case definition with more specificity

is needed for accurate case detection. In the absence of a more specific case definition, continued emphasis on confirmatory laboratory-based diagnostics is warranted.

10.1371/journal.pntd.0005857 this link

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76. **Evaluation of the GeneXpert for Human Monkeypox Diagnosis.**
Li Daniel The American journal of tropical medicine and hygiene 2017;96(2):405-410.

Monkeypox virus (MPXV), a zoonotic orthopoxvirus (OPX), is endemic in the Democratic Republic of Congo (DRC). Currently, diagnostic assays for human monkeypox (MPX) focus on real-time quantitative polymerase chain reaction (PCR) assays, which are typically performed in sophisticated laboratory settings. Herein, we evaluated the accuracy and utility of a multiplex MPX assay using the GeneXpert platform, a portable rapid diagnostic device that may serve as a point-of-care test to diagnose infections in endemic areas. The multiplex MPX/OPX assay includes a MPX-specific PCR test, OPX-generic PCR test, and an internal control PCR test. In total, 164 diagnostic specimens (50 crusts and 114 vesicular swabs) were collected from suspected MPX cases in Tshuapa Province, DRC, under national surveillance guidelines. The specimens were tested with the GeneXpert MPX/OPX assay and an OPX PCR assay at the Institut National de Recherche Biomedicale (INRB) in Kinshasa. Aliquots of each specimen were tested in parallel with a MPX-specific PCR assay at the Centers for Disease Control and Prevention. The results of the MPX PCR were used as the gold standard for all analyses. The GeneXpert MPX/OPX assay performed at INRB had a sensitivity of 98.8% and specificity of 100%. The GeneXpert assay performed well with both crust and vesicle samples. The GeneXpert MPX/OPX test incorporates a simple methodology that performs well in both laboratory and field conditions, suggesting its viability as a diagnostic platform that may expand and expedite current MPX detection capabilities. Copyright © The American Society of Tropical Medicine and Hygiene.

10.4269/ajtmh.16-0567 this link

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77. **Evolution of a Disease Surveillance System: An Increase in Reporting of Human Monkeypox Disease in the Democratic Republic of the Congo, 2001-2013.**
Hoff Nicole A. International journal of tropical disease & health 2017;25(2):No page numbers.

OBJECTIVE: Evaluating the effectiveness of a surveillance system, and how it improves over time has significant implications for disease control and prevention. In the Democratic Republic of Congo (DRC), the Integrated Disease Surveillance and Response (IDSR) was implemented to estimate the burden of disease, monitor changes in disease occurrence, and inform resource allocation. For this effort we utilized national passive surveillance data from DRC's IDSR to explore reporting trends of human monkeypox (MPX) from 2001 to 2013., METHODS: We obtained surveillance data on MPX cases occurring between January 2001 and December 2013 from the DRC Ministry of Health (MoH). Phases of the surveillance system, yearly trends in reporting and estimated incidence for MPX were analyzed using SAS v9.2 and Health Mapper., RESULTS: Between 2001 and 2013, three discrete surveillance phases were identified that described the evolution of the surveillance system. Overall, an increase in suspected MPX cases was reported, beyond what would be expected from simply an improved reporting system. When restricting the analysis to the "stable phase," national estimated incidence increased from 2.13 per 100,000 in 2008 to

2.84 per 100,000 in 2013., CONCLUSIONS: The reported increase in MPX, based on an evolving surveillance system, is likely to be a true increase in disease occurrence rather than simply improvements to the surveillance system. Further analyses should provide critical information for improved prevention and control strategies and highlight areas of improvement for future data collection efforts.

10.9734/IJTDH/2017/35885 this link

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78. **Frameworks for Preventing, Detecting, and Controlling Zoonotic Diseases.**
Shiferaw Miriam L. Emerging infectious diseases 2017;23(13):No page numbers.

Preventing zoonotic diseases requires coordinated actions by government authorities responsible for human and animal health. Constructing the frameworks needed to foster intersectoral collaboration can be approached in many ways. We highlight 3 examples of approaches to implement zoonotic disease prevention and control programs. The first, rabies control in Ethiopia, was implemented using an umbrella approach: a comprehensive program designed for accelerated impact. The second, a monkeypox program in Democratic Republic of the Congo, was implemented in a stepwise manner, whereby incremental improvements and activities were incorporated into the program. The third approach, a pathogen discovery program, applied in the country of Georgia, was designed to characterize and understand the ecology, epidemiology, and pathogenesis of a new zoonotic pathogen. No one approach is superior, but various factors should be taken into account during design, planning, and implementation.

10.3201/eid2313.170601 this link

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79. **Maternal and Fetal Outcomes Among Pregnant Women With Human Monkeypox Infection in the Democratic Republic of Congo.**
Mbala Placide K. The Journal of infectious diseases 2017;216(7):824-828.

Human monkeypox is an endemic disease in rain-forested regions of central Democratic Republic of Congo. We report fetal outcomes for 1 of 4 pregnant women who participated in an observational study at the General Hospital of Kole (Sankuru Province), where 222 symptomatic subjects were followed between 2007 and 2011. Of the 4 pregnant women, 1 gave birth to a healthy infant, 2 had miscarriages in the first trimester, and 1 had fetal death, with the macerated stillborn showing diffuse cutaneous maculopapillary skin lesions involving the head, trunk and extremities, including palms of hands and soles of feet.

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80. **Monkeypox Virus Host Factor Screen Using Haploid Cells Identifies Essential Role of GARP Complex in Extracellular Virus Formation.**
Realegeno Susan Journal of virology 2017;91(11):No page numbers.

Monkeypox virus (MPXV) is a human pathogen that is a member of the Orthopoxvirus genus, which includes Vaccinia virus and Variola virus (the causative agent of smallpox). Human monkeypox is considered an emerging zoonotic infectious disease. To identify host factors required for MPXV infection, we performed a genome-wide insertional mutagenesis screen in human haploid cells. The screen revealed several candidate genes, including those involved in Golgi trafficking, glycosaminoglycan biosynthesis, and glycosylphosphatidylinositol (GPI)-anchor biosynthesis. We validated the role of a set of vacuolar protein sorting (VPS) genes during infection, VPS51 to VPS54 (VPS51-54), which comprise the Golgi-associated retrograde protein (GARP) complex. The GARP complex is a tethering complex involved in retrograde transport of endosomes to the trans-Golgi apparatus. Our data demonstrate that VPS52 and VPS54 were dispensable for mature virion (MV) production but were required for extracellular virus (EV) formation. For comparison, a known antiviral compound, ST-246, was used in our experiments, demonstrating that EV titers in VPS52 and VPS54 knockout (KO) cells were comparable to levels exhibited by ST-246-treated wild-type cells. Confocal microscopy was used to examine actin tail formation, one of the viral egress mechanisms for cell-to-cell dissemination, and revealed an absence of actin tails in VPS52KO- or VPS54KO-infected cells. Further evaluation of these cells by electron microscopy demonstrated a decrease in levels of wrapped viruses (WVs) compared to those seen with the wild-type control. Collectively, our data demonstrate the role of GARP complex genes in double-membrane wrapping of MVs necessary for EV formation, implicating the host endosomal trafficking pathway in orthopoxvirus infection. IMPORTANCE Human monkeypox is an emerging zoonotic infectious disease caused by Monkeypox virus (MPXV). Of the two MPXV clades, the Congo Basin strain is associated with severe disease, increased mortality, and increased human-to-human transmission relative to the West African strain. Monkeypox is endemic in regions of western and central Africa but was introduced into the United States in 2003 from the importation of infected animals. The threat of MPXV and other orthopoxviruses is increasing due to the absence of routine smallpox vaccination leading to a higher proportion of naive populations. In this study, we have identified and validated candidate genes that are required for MPXV infection, specifically, those associated with the Golgi-associated retrograde protein (GARP) complex. Identifying host targets required for infection that prevents extracellular virus formation such as the GARP complex or the retrograde pathway can provide a potential target for antiviral therapy. Copyright © 2017 American Society for Microbiology.

10.1128/JVI.00011-17 this link

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81. **Presumptive risk factors for monkeypox in rural communities in the Democratic Republic of the Congo.**
Quiner Claire A. PloS one 2017;12(2):e0168664.

Monkeypox virus (MPXV), a close relative of Variola virus, is a zoonotic virus with an unknown reservoir. Interaction with infected wildlife, bites from peri-domestic animals, and bushmeat hunting are hypothesized routes of infection from wildlife to humans. Using a Risk Questionnaire, performed in monkeypox-affected areas of rural Democratic Republic of the Congo, we describe the lifestyles and demographics associated with presumptive risk factors for MPXV infection. We generated two indices to assess risk: Household Materials Index (HMI), a proxy for socioeconomic status of households and Risk Activity Index (RAI), which describes presumptive risk for animal-to-human transmission of MPXV. Based on participant self-reported activity patterns, we found that people in this population are more likely to visit the forest than a market to fulfill material needs, and that the reported occupation is limited in describing behavior of individuals may participate. Being bitten by rodents in the home was commonly reported, and this was significantly associated with a low HMI. The highest scoring RAI sub-groups were 'hunters' and males aged >= 18 years; however, several activities involving MPXV-implicated animals were distributed across all

sub-groups. The current analysis may be useful in identifying at-risk groups and help to direct education, outreach and prevention efforts more efficiently.

10.1371/journal.pone.0168664 this link

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82. **Toward Understanding the Outcomes of Monkeypox Infection in Human Pregnancy.**
Kisalu Neville K. The Journal of infectious diseases 2017;216(7):795-797.

10.1093/infdis/jix342 this link

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83. **Varicella Coinfection in Patients with Active Monkeypox in the Democratic Republic of the Congo.**
Hoff Nicole A. EcoHealth 2017;14(3):564-574.

From 2006 to 2007, an active surveillance program for human monkeypox (MPX) in the Democratic Republic of the Congo identified 151 cases of coinfection with monkeypox virus and varicella zoster virus from 1158 suspected cases of human MPX (13%). Using clinical and socio-demographic data collected with standardized instruments by trained, local nurse supervisors, we examined a variety of hypotheses to explain the unexpectedly high proportion of coinfections among the sample, including the hypothesis that the two viruses occur independently. The probabilities of disease incidence and selection necessary to yield the observed sample proportion of coinfections under an assumption of independence are plausible given what is known and assumed about human MPX incidence. Cases of human MPX are expected to be underreported, and more coinfections are expected with improved surveillance.

10.1007/s10393-017-1266-5 this link

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